A STUDY ON THE LOWER RESPIRATORY TRACT INFECTIONS IN POST RENAL TRANSPLANT PATIENTS ATTENDING THE NEPHROLOGY DEPARTMENT IN A TERTIARY CARE HOSPITAL WITH SPECIAL REFERENCE TO OPPORTUNISTIC INFECTIONS

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CERTIFICATE

This is to certify that this dissertation entitled "**A STUDY ON THE LOWER RESPIRATORY TRACT INFECTIONS IN POST RENAL TRANSPLANT PATIENTS ATTENDING THE NEPHROLOGY DEPARTMENT IN A TERTIARY CARE HOSPITAL WITH SPECIAL REFERENCE TO OPPORTUNISTIC INFECTIONS"** is the bonafide original work done by **Dr. A. ILAKKIYA,** MD Post graduate in Microbiology (2013-2016), under my overall supervision and guidance in the department of Microbiology, Stanley Medical College, Chennai, in partial fulfillment of the regulations of The Tamil Nadu Dr. M.G.R. Medical University for the award of **M.D Degree in Microbiology (Branch IV).**

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DECLARATION

I solemnly declare that this dissertation "**A STUDY ON THE LOWER RESPIRATORY TRACT INFECTIONS IN POST RENAL TRANSPLANT PATIENTS ATTENDING THE NEPHROLOGY DEPARTMENT IN A TERTIARY CARE HOSPITAL WITH SPECIAL REFERENCE TO OPPORTUNISTIC INFECTIONS"** is the bonafide work done by me during my post graduate course in MD Microbiology (2013-2016) at the Department of Microbiology, Govt. Stanley Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. R. SELVI, M.D.,** Professor of Microbiology, Govt. Stanley Medical College, Chennai, 600 001. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University**, Chennai in partial fulfillment of the University regulations for the award of degree of **M.D. Branch IV Microbiology** examinations to be held in April 2016.

Place: Chennai **Dr. A. ILAKKIYA**

Date: APRIL 2016

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CONTENTS

ABSTRACT

A STUDY ON THE LOWER RESPIRATORY TRACT INFECTIONS IN POST RENAL TRANSPLANT PATIENTS ATTENDING THE NEPHROLOGY DEPARTMENT IN A TERTIARY CARE HOSPITAL WITH SPECIAL REFERENCE TO OPPORTUNISTIC INFECTIONS

INTRODUCTION:

Infection is of major concern in renal transplant recipients as this creates a vicious cycle . Infection leads to rejection and rejection in turn leads to infection. Pneumonia is the second leading cause of infection in renal transplant recipients , (2.9-30%)[7,8,9] after urinary tract infection (23.6%) [13]. This study deals with the prevalence of lower respiratory tract infection in post renal transplant recipients in our hospital.

AIIMS @ OBJECTIVES:

To determine the prevalence of lower respiratory tract infections in post renal transplant recipients and its association with risk factors,

To look for the type of organism causing pneumonia and its relation with duration of transplant,

To determine the antibiotic susceptibility pattern of bacterial infections.

MATERIALS & METHODS

Type of study:

Both prospective and retrospective study

Place of Study & Period of Study:

Department of Microbiology, Stanley Medical college,

Department of Nephrology, Stanley Medical college.

Study period:

September 2014 to August 2015.

Sample size and Inclusion criteria:

A total of 147 post renal transplant recipients who are followed as inpatients and outpatients in the Department of Nephrology, Stanley Medical College were taken for the study. The details of lower respiratory tract infection that occurred previously is collected from the patient's record and the newer samples were also collected and processed from the patients with symptoms and signs of respiratory tract infection .

Ethical Consideration

Ethical and research clearance was obtained from the Ethical committee, Stanley Medical College.

Statistical Analysis

The collected data was analyzed with SPSS 21.0 version.

CONCLUSION

The prevalence of lower respiratory tract infection in renal transplant recipients in our hospital is about 27.2%.

There was a higher incidence of fungal pneumonia in poorly controlled diabetes patients.

Patients who received intravenous pulse methyl prednisolone for rejection had higher incidence of bacterial infection.

Induction therapy was not associated with increase in incidence of infection.

Since patient is on lifelong prophylaxis of cotrimoxazole, there is a higher increase of resistance to it.

INTRODUCTION

Transplantation medicine is one of the most challenging and complex areas of modern medicine. The use of solid organ transplantation has been established as accepted therapy for end-stage disease of the kidneys, liver, heart and lungs for nearly 30 years. According to the data provided by the Global Observatory on Donation and Transplantation (GODT) 114,690 solid organs are transplanted in 2012. Living kidney transplants constitutes about 42.3% of the transplants.

Renal transplantation is the transfer of kidney into a person with end stage renal disease which is defined by Glomerular filtration rate < 15ml/min/1.73sqmm. End stage disease of the kidney is most commonly caused by malignant hypertension, diabetes mellitus, infection, focal segmental glomerulosclerosis, polycystic kidney disease, inborn errors of metabolism, systemic lupus erythematosus. Most of the renal transplant recipients are on dialysis at the time of transplant.

Though renal transplantation is considered the most novel approach in treating a patient with end stage renal disease, rejection is a major concern. The recipient's immune system attacks the donor organ as foreign substance since it cannot discriminate between harmful substances like bacteria, viruses, fungi and the transplanted organ. Here comes the role of immunosuppressive agents to control the body's immune response. For the long term survival of both the graft and the recipients of both the living and deceased donor transplant recipients, almost all patients require life time immunosuppression and hence are at increased risk of infection any time during their life period.

Infection is of major concern in renal transplant recipients as this creates a vicious cycle . Infection leads to rejection and rejection in turn leads to infection. Since pneumonia is the second leading cause of infection in renal transplant recipients , (2.9-30%)[7,8,9] after urinary tract infection (23.6%) [13], knowledge about its prevalence, the type of organism causing, its pattern of resistance, the duration of its occurrence time since transplant, its association with various immunosuppressive drugs need to be known. Though there are various studies describing about them, it cannot be universally applied, since each hospital follows a different protocol to treat the renal transplant recipients.

Hence this study deals with the prevalence of lower respiratory tract infection in post renal transplant recipients in our hospital. The transplant recipients receive induction agents and increased dose of maintenance immunosuppressive regimens during the initial period. Anti rejection therapy for acute rejection is given within three months of transplant as they occur most commonly during this period. Hence the study population is divided into 4 groups based on the time since transplant

1) Immediate post operative period,

2) Within 2 months,

3) >2 months to <2 years,

4) >2 years which will enable to correlate the infection with the degree of immunosuppression the patient had received during that period.

AIMS & OBJECTIVES

1. To determine the prevalence of lower respiratory tract infections in post renal transplant recipients and its association with risk factors,
2. To look for the type of organism causing pneumonia and its relation with duration of transplant,
3. To determine the antibiotic susceptibility pattern of bacterial infections.

REVIEW OF LITERATURE

Organ transplantation is the transfer of an organ from one person to another or from one site to another site of the same person or a different person in order to replace the recipient's damaged or absent organ.

Types of transplant: Brenner @ Rector [80]

Autograft:

It is the transplantation of organ to the same person. There will be no mounting of immune response against the transplanted organ

Allograft:

It is the transplantation of organ between genetically non identical members of the same species i.e the donor and the recipient. The immune system of the recipient identifies the donor organ as foreign and mounts an immune response to destroy it.

Isograft:

It is the transplantation of organ between identical twins. Here the recipient's body doesn't mount an immune response.

Xenograft:

It is the transplantation of organ between members of different species. There is an increased risk of non-compatibility, rejection, and disease carried in the tissue.

Based on the source of the donor , renal transplantation is classified as

1) Living donor renal transplant, which is further divided as

a)Living related

b)Living unrelated based on the biological relationship between the donor and the recipient.

2) Deceased /cadaveric donor renal transplant

Living Donor renal transplant:

In this type of transplant, the donor is an alive individual and he donates his organ or its part to a recipient. In this type of transplantation , the graft survival and function will be excellent and the rejection rate will be lower compared to the deceased donor transplantation. Hence the immunosuppression used will be less aggressive and the infection rate will be lower in comparison with the deceased organ transplantation. This difference is also seen between a living related and unrelated donor renal transplants as the rejection rate will be lower in related donor transplants.

Deceased Donor transplant:

Here the donor is a deceased person who is brain dead and who are maintained viable by ventilators. In this type of transplantation the graft survival and function will be somewhat lower and the rejection rate will be higher compared to the living donor transplantation. Hence the immunosuppression used will be more aggressive and the infection rate will be higher in comparison with the living organ transplantation.

Classification of immunosuppressive drugs:

1. Induction therapy,

2. Maintenance therapy,
3. Anti rejection therapy.

Induction therapy:

Induction therapy is treatment with a biological agent either a biological agent either a lymphocyte depleting agent or an interleukin 2 receptor antagonist given before, at the time of or immediately after transplantation. It depletes or modulates T cell responses at the time of antigen presentation. It increases immunosuppressive efficacy by preventing acute rejection or by enabling reduction of other components of regimen like calcineurin inhibitors or corticosteroids.

Protein drugs:

Depleting antibodies (against T cells, B cells, or both)

- Polyclonal antibody: horse or rabbit antithymocyte globulin
- Mouse monoclonal anti-CD3 antibody (muromonab-CD3)
- Humanized monoclonal anti CD-52 antibody (alemtuzumab)
- B-cell-depleting monoclonal anti-CD-20 antibody (rituximab)
- Nondepleting antibodies and fusion proteins
- Humanized or chimeric monoclonal anti-CD25 antibody (daclizumab, basiliximab)
- Fusion protein with natural binding properties: CTLA4-Ig (Belatacept)

Intravenous gammaglobulin

C5 inhibitor

Eculizumab

Protease inhibitor

Bortezomib

Maintenance immunosuppressive therapy:

It is a long term treatment to prevent acute rejection and deterioration of graft function. The therapy is started before or at the time of transplant and the initial medication may or may not be used with induction therapy. Maintenance immunosuppressive drugs are used in combination to minimise the toxicity that is associated with each drug. Since the risk of acute rejection is highest in the first three months after transplant, higher doses are used during this time and the dose of these drugs are reduced thereafter. The maintenance immunosuppression is used for all patients lifelong.

Glucocorticoids

Small-molecule drugs

Immunophilin-binding drugs

Calcineurin inhibitors

Cyclophilin-binding drugs: cyclosporine

FKB12-binding drugs: tacrolimus, modified release tacrolimus

Target-of-rapamycin inhibitors: sirolimus, everolimus

Inhibitors of nucleotide synthesis

- Purine synthesis (IMDH) inhibitors
- Mycophenolate mofetil
- Enteric-coated mycophenolic acid (EC-MFS)
- Mizoribine (MZR)
- Pyrimidine synthesis (DHODH) inhibitors
- Leflunomide
- FK778
- Antimetabolites: azathioprine (Aza)
- Sphingosine-1-phosphate-receptor antagonists: FTY720

Protein drugs

Depleting antibodies (against T cells, B cells, or both)

- Polyclonal antibody: horse or rabbit antithymocyte globulin
- Mouse monoclonal anti-CD3 antibody (muromonab-CD3)

- Humanized monoclonal anti CD-52 antibody (alemtuzumab)
- B-cell-depleting monoclonal anti-CD-20 antibody (rituximab)

Nondepleting antibodies and fusion proteins

- Humanized or chimeric monoclonal anti-CD25 antibody (daclizumab, basiliximab)
- Fusion protein with natural binding properties: CTLA4-Ig (Belatacept)

Intravenous gammaglobulin

C5 inhibitor

Eculizumab

Protease inhibitor

Bortezomib

Antirejection therapy: (Acute rejection)

These agents are used to treat acute rejection. There are two types of acute organ rejection.

a) Cell mediated rejection

b) Antibody mediated rejection

Agents used to treat acute rejection are steroid pulse, antithymocyte globulin, muromonab CD3

Immunosuppressive regimen protocol Stanley Medical College:

Induction agent:

The immunosuppressive regimen starts with an induction agent for deceased and spousal transplants (high risk transplants) with either a lymphocyte depleting agent Anti thymocyte globulin in a single dose of 1.5mg/kg in an infusion for 4-6hrs perioperatively or a T cell non depleting monoclonal antibody against IL2 receptor Basiliximab ,20mg infusion for 30 minutes on day 0 and day 4. Live related renal transplants and patients with risk of sepsis in high risk transplants are not given induction.

Intraoperatively 1gm pulse methyl prednisolone is given intravenously before clamp release of the renal vessels .

Maintenance therapy:

A triple immunosuppressive regimen is started from day 0 for maintenance therapy and given lifelong. It includes Tacrolimus (0.1mg/kg/day) and its trough level in blood is maintained at 8-10 ng/ml upto 30 days. Then the dose is gradually tapered to maintain at 7-8ng/ml for the first three months and at 6-7ng/ml for the next three

months (2nd month- 7th month).Then the dosage is adjusted to maintain a trough level of 3-5ng/ml life time.

The second drug is Mycophenolate Mofetil. It is given in a dosage of 1gm/day (<50 kgs), 1.25gm/day (50-60kgs) or 1.5g/day(>60kgs) lifelong.

The third drug is oral prednisolone given in a dose of 0.5mg/kg/day up to 20 days .Then it is tapered to 20mg and given for next 15 days and tapered to 15mg for next 15 days. Then the drug is given in a dosage of 7.5mg-10mg according to the body weight lifelong.

The dosage is not fixed and is individualised according to the therapeutic effect needed and for reducing the adverse affect.

Anti rejection therapy:

For patients with rejection, low dose intravenous pulse methyl prednisolone (250mg-500mg) is given for 3-5 days.

Prophylaxis for Pneumocystis carinii:

Cotrimoxazole is given life long

Prophylaxis for CMV:

Valgancyclovir 450mg od is given for 3 months for patients who were given Anti Thymocyte Globulin.

Effects of immunosuppressive agents:

Immunosuppressive agents causes 3 major effects

1) The intended therapeutic effect of suppressing rejection
2) The deleterious acquired immunodeficiency that the host sustains leading to increased risk of infection or malignancy
3) The direct or indirect toxicity to the tissues

Infection and immunosuppression:

The immunosuppressive agents used in transplantation targets single or multiple sites of the immune system and helps in preventing rejection. So they play a double edged sword impairing the recipient's immune response thereby predisposing them to a variety of pathogens. All the major immune defence mechanism including the anatomical barrier, innate immunity, acquired immunity is breached resulting in opportunistic infection. They cause drug induced anti proliferative capacity leading anti proliferative capacity leading to erosion of mucosal barrier, transient cytopenia, hyperglycemia, uremia, malnutrition, use of invasive devices leading to trauma, colonisation , infection.

While surgical procedures are well established, the field of transplantation continues to explore and experience innovations in immunosuppressive therapy with goals of improving outcomes and in pursuit of tolerance. [34]The positive effects of the immunosuppressive agents, obligatory for the prevention of organ rejection, have been tempered by the negative effects of these same therapies, leading to various infections that range in both frequency and severity.[35] Newer immunomodulating agents have been developed, increasing the number of therapies that prevent organ rejection.

However, this has simultaneously created newer unwanted opportunities for pathogens to cause infectious complications.[36,37]

Infection in post renal transplant recipients:

Urinary tract infections were the most common infection (23.6%) 13followed by pulmonary infections in case of renal transplant recipients.

Incidence of Pneumonia in renal transplant recipients:

The incidence of pneumonia is highest in lung transplant recipients of about 72% [1] followed by heart (17-28%) [2,3,4] and liver (8-23%) [5,6] and kidney (2.9-30%) transplant recipients [7,8,9].The incidence of pulmonary infection is lowest in kidney transplant recipients, reflecting the less rigorous surgical procedure required to implant the allograft and the decreased level of immunosuppression required to maintain it.[10]

Perioperative complications: renal transplantation.

Renal transplantation is done with low perioperative pulmonary complications due to the use of a lower abdominal incision and relatively a better health of the transplant recipients [11,12]. Most of the patients are extubated in the operating room. Pulmonary edema is the most common non infectious pulmonary complication due to impairment of salt and water excretion in the setting of early allograft dysfunction or rejection. Risk of thromboembolic events due to pelvic vein manipulation during surgery may occur[11].

Gender difference among renal transplant recipients with LRTI:

The percentage of pulmonary infection was more in males about 83.4% compared to females16.5% according to a study conducted by R Ram, KV Dakshina Murty, N Prasad Department of Nephrology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad[13]

Age group:

According to a study conducted in Hyderabad , most of the patients fall in the age group of 20-39 years(53.8%) and this age group had maximum number of infections followed by 40-59 years age group (34.3%) , 0-19 years(8.7%) and >60 years group(1.7%) [13]

Spectrum of infections in renal transplant recipients:

Bacterial pneumonia in renal transplant recipients:

Bacteria is the most common cause of lower respiratory tract infections in solid organ transplant recipients [21,22,23,24]. It is more common in cardiac (15%) transplants followed by liver (9%) and kidney (4-6%) transplant recipients .In liver and kidney transplant recipients the mortality due to pneumonia was 21% and 35%, respectively. [25].

Infection by nosocomial pathogens constitutes most of the infection in the initial perioperative period which includes *Pseudomonas aeruginosa, Acinetobacter* species, and *Staphylococcus aureus , Escheria coli, Klebsiella* species . The risk for nosocomial pneumonia is increased if the duration of mechanical ventilation is prolonged following transplant After the initial post-transplant period,

community acquired pathogens including *Haemophilus influenza*, *Streptococcus pneumonia*, and *Legionella* species predominate. With the use of trimethoprim-sulfamethoxazole for the prophylaxis of pnemocystis carinii, the incidence of *Nocardia* pneumonia is very much reduced. Nosocomial and community acquired pneumonia constitutes about 58% and 8% mortality respectively. Mechanical ventilation and nosocomial infection are increased risk factors for morality associated with pneumonia [25]

Pulmonary tuberculosis in renal transplant recipients:

Incidence of tuberculosis in SOT:

The incidence of *M. tuberculosis* in solid organ transplant recipients is 30 to 100-times higher than in the general population. In endemic areas the incidence of mycobacterium tuberculosis in solid organ transplants is 15% [25.]The incidence of tuberculosis in renal allograft recipient is 12.3% [41]

Median time to develop TB:

The median time to develop tuberculosis is 20 months as per the study conducted by JIA Liu and his colleagues.[38] A global review on TB estimated the median time for onset at nine months post transplantation.[39]Immunosuppression with tacrolimus or mycophenolate has been associated with the development of TB earlier in the post transplantation period and at a higher frequency within 6 months .40Lung is the most common organ affected(62.2% ie 1.6% cases of pulmonary tuberculosis

among the transplant recipients).[38].Majority of tuberculosis occurs within one year [42,43,44] of post transplant.

Risk factors for tuberculosis:

Risk factor
Immunosuppressive therapy[a]
OKT3 or anti-T lymphocyte antibodies (III)
Intensification of immunosuppression associated with graft rejection (II)
Cyclosporine A vs. azathioprine plus prednisone (II)
Mycophenolate mofetil and tacrolimus vs. azathioprine, cyclosporine, and prednisone (III)
History of exposure to *Mycobacterium tuberculosis*
Positive PPD test result (III)
Radiological evidence of previous untreated TB (III)
Clinical condition
Chronic renal insufficiency or hemodialysis (kidney transplantation; II)
Diabetes mellitus (II)
Hepatitis C virus infection (kidney transplantation; III)
Chronic liver disease (III)
Other coexisting infections: profound mycoses, cytomegalovirus, or *Pneumocystis jiroveci* or *Nocardia* pneumonia (III)

NOTE. Roman numerals indicate the degree of evidence (table 1). PPD, purified protein derivative. [45,46,49]

Diabetes and Tuberculosis:

According to a study conducted in Christian Medical College Vellore, diabetes mellitus, PTDM ,chronic liver disease, and the occurrence of other coexisting infections such as deep mycoses, CMV, PCP, Nocardia are important risk factors for post transplant Tuberculosis in renal transplant recipients.[48]

HCV and Tuberculosis:

According to a study conducted in University hospital Spain, Hepatitis C virus infection is an important risk for tuberculosis in post renal transplant recipients. The

patients with HCV infection had higher percentage of tuberculosis infection than in the controls.[47]

Reactivation of latent infection is the most common cause of infection and primary infection and transmission from the donor allograft also occurs. In tuberculosis infection the most common organ affected are the lungs. Though fever is the common presentation it is not universally present. Focal infiltrate, miliary pattern, cavitary disease, diffuse infiltrates, and pleural effusions are the radiographic presentations .[25]

Fungal pneumonia in renal transplant recipients:

Incidence of fungal pneumonia:

Two contemporary studies in liver and kidney transplant recipients found the incidence of fungal pneumonia (not including *pneumocystis jirovecii*) ranges between 8 and 17% [22]. Another study conclude that pulmonary infections in kidney transplant recipients is about 1 to 4% [21,27]. Even though the occurrence of fungal pneumonia is lower than bacterial pneumonia in transplant recipients, fungal pneumonia carries a higher mortality rate of 80-100% when disease becomes invasive [28, 29].

Risk factors causing fungal pneumonia in renal transplant recipients:

Invasive fungal infection occurs in renal transplant recipients due to various risk factors which include the host and environmental factors:

- renal failure,
- post operative complications,
- frequent bacterial infection,

- recurrent intensified immunosuppression
- people in older age group, [28]
- environmental exposure,
- colonization with pathogenic fungi,
- use of antifungal prophylaxis,
- net state of immunosuppression which includes anti rejection therapies, breaches in mucocutaneous barriers, leukopenia, comorbid conditions (e.g., malnutrition, cirrhosis, diabetes mellitus and hypogammaglobulinemia) and chronic viral infections (e.g., CMV, HCV, HBV and HIV) [31]

Organisms causing fungal infection:

Candida *(35-91%) or* Aspergillus species (9-52%) is the most common fungal infection affecting lungs in transplant recipients.[29]

Candida:

According to the study conducted by Pugliese F and his colleagues , most of the nosocomial fungal colonization or infection in solid organ transplant patients is caused by Candida spp (98%) in a transplant ICU [30]. Candidal infection was associated with a longer stay in the intensive care unit (30 vs. 5 days) and increased mortality (35% vs. 3.5%) than patients without *Candida* infection.

Aspergillus spp:

Aspergillus sp. is a saprophytic fungal organism . It causes more serious infection and increased mortality than *Candida sp*. In a case control study conducted by Gavalda J and his colleagues, the overall incidence of invasive Aspergillus fungal infection was found to be 1.4% in over 11,000 patients and is about 0.2% in renal transplant recipients [28]. The mortality rate for invasive Aspergillosis patients was about 54% . Most of the invasive Aspergillosis cases occurred within the first 90 days. The risk factors associated with earlier infection were complicated postoperative course, recurrent bacterial infections or CMV disease and renal failure. Patients who developed later disease were older and they had intense immunosuppression and renal failure.

Other organisms:

Other opportunistic fungal infections which causes pneumonia include scedosporium, fusarium, cladosporium, rhizopus, and mucor species [60]. The mortality was about 55% for non aspergillus mycelial infection. The mortality rate was 80-100% in patients with zygomycosis (rhizopus andmucor species) or non-aspergillus hyalohyphomycosis (scedosporium

Mucormycosis:

In solid organ transplantation Mucormycosis causes invasive fungal infections in a small proportion of patients. But it causes a very high mortality rate. The range of incidence of mucormycosis is about 0.2%– 1.2% in renal transplant recipients. .In a retrospective study conducted by Singh N , neutropenia, acidosis with and without hyperglycemia and deferoxamine (DFO) use were absent in solid organ transplant

recipients [75] but all patients were under chronic immunosuppression, with high doses of systemic corticosteroids and dissemination to distant organs has occurred after rejection and its treatment. In a prospective, matched, case-controlled study of mucormycosis in solid organ transplant recipient patients, renal failure, diabetes mellitus, and prior voriconazole and/or caspofungin were associated with an increased risk of mucormycosis [76]. But tacrolimus was associated with a decreased risk for mucormycosis.. Median time to develop mucormycosis was about 5.7 months.

Diabetes Mellitus and Ketoacidosis- important risk factors for mucormycosis. [32]

In many of the studies, diabetes mellitus is reported as a predisposing factor for the development of mucormycosis(36%–88%) [63, 64–73]. Patients with uncontrolled hyperglycemia, particularly those with ketoacidosis, are more prone to develop mucormycosis. [69, 70,74]. In some patients, Mucormycosis may be the first manifestation with undiagnosed diabetes mellitus [72], but it is hardly noted in those patients with diabetes under control [62]. Type 1, type 2, and secondary diabetes mellitus are all reportedly risk factors for mucormycosis [73.]

Endemic dimorphic Fungus:

Dimorphic fungi such as Coccidioides immitis, histoplasma capsulatum and blastomyces dermatitidis have also been reported[77]. Patients with blastomycosis frequently present with respiratory failure (78%) but fortunately the incidence of blastomycosis in solid organ transplant recipients is only 0.14% which is lower than that of histoplasmosis (0.4-2.1%) or coccidioidomycosis (0.59-8.7%)

[77]. Cryptococcus accounts for 3% of invasive fungal infections in SOT recipients but is associated with a mortality of up to 40% [78]

Pneumocystis jirovecii

Before the use of trimethoprim-sulfamethoxazole (TMP-SMX) , the incidence of pneumocystis jirovecii (formerly pneumocystis carinii) pneumonia (PCP) infection ranged between 15% and 88% in heart-lung recipients and 0.6 to 11.5% in renal transplant patients .Infection usually develops between three and 6 months post transplant when the immunosuppression is maximum. Recent evidence suggest that rituximab use for treatment of acute humoral rejection had lead to PCP pneumonia in renal transplant recipients.[22]

Immunosuppressive regimens:

Induction agents:

T cell depleting agent: Anti thymocyte globulin:.

Mechanism of Action

Anti thymocyte globulin is a polyclonal antibody which is produced by the infusion of human T cells into horse or rabbit . It causes dose dependent depletion of T-cells and it also has effect on B cells, natural killer cells, regulatory T cells and dendritic cells. The degree of depletion of T-cells is dependent on the total dose of the drug administered and also on the duration the therapy is being given. Usually the course of therapy is 3-5 days and it may range from 1-10 days [50]

Side Effects

Anti thymocyte globulin can cause infusion related symptoms like fever, hypotension, rashes, chills. It also causes CHF, serum sickness, eosinophilia or leucopenia, thrombocytopenia. [51,52,53].

Duration of Effect

Rabbit- Anti thymocyte globulin has a long half life of about 30 days but CD3 lymphopenia may last up to one year. Human- Anti thymocyte globulin has a less intense CD3 suppression and has and a shorter duration of effect and lymphopenia usually resolves in about 14 days) [54].

General Infectious Disease Issues

Several studies have compared the effect of R-ATG with H-ATG. In one study, 56% of patients who were treated with R-ATG developed infection during the first year after transplant as compared to 75% with H-ATG. In a study conducted by Cinacio G and his colleagues patients received ATG is compared with patients who received alemtuzumab or daclizumab for induction during renal transplantation. It showed a infection rate of 27% in each group with 3 cases of Cytomegalovirus and 1 case of BK virus nephropathy [55].

Bacterial Infection

The effect of Anti thymocyte globulin on bacterial infections is not clearly defined in any of the studies. In renal transplant recipients there is increase in incidence of urinary tract infections and wound infections. In a study conducted by

Midtvedt K and his colleagues ATG has been associated with increased incidence of pneumonia, bacteremia or sepsis [56]. Studies conducted on lymphocyte depleting therapy (including both alemtuzumab and anti-thymocyte globulin) have showed no association with Nocardia infections whereas high dose steroids, Cytomegalovirus infection and high calcineurin inhibitor levels were associated with Nocardia infection[57].

Fungal Infections

Generally ATG induction in renal transplants does not lead to any increase in incidence of fungal infection. Anti-rejection utilization does There is also no increase in risk if ATG is used as rejection therapy. But ATG causes increased risk for Pneumocystis carinii pneumonia when no prophylaxis has been given. False positive Histoplasma urine antigens have been identified in those who have received R-ATG. Cryptococcosis was associated when two doses of R-ATG is given but not when1 dose is given for renal ransplants. The median time for diagnosis was 255 days and the death rate was 14.2% [58]. Anti thymocyte globulin is not associated with zygomycetes infection while renal failure, diabetes, prior voriconazole or caspofungin use were. Tacrolimus lowered the risk of zygomycosis infection [59].

L-2 receptor antagonist (basiliximab)

Mechanism of Action

Basiliximab (Simulect) is a chimeric murine-human monoclonal antibody that binds selectively to the alpha chain (CD25) of the IL-2 receptor.. IL-2 is a leukocytotrophic hormone that is instrumental in the body's natural response to

microbial infection and cannot discriminate between foreign and self. CD25 is a type I transmembrane protein present on activated T-cells, activated B-cells, some thymocytes, myeloid precursors and oligodendrocytes. CD25 associates with CD122 to for a high affinity receptor for IL-2. Resting lymphocytes are not targeted by IL-2 receptor antagonists. CD25 participates in lymphocyte differentiation, activation, and proliferation. At this time, these medications are used mostly for solid organ induction in recipients who are low risk for rejection.

Duration of Effect:

The half life of basiliximab is long about 13.4 days in adults and for about 9.4 days in children. Basiliximab completely saturates the interleukin-2 receptor for a period of about 4-6 weeks in adult renal transplant recipients and for about 42 days in pediatric recipients.

Infection and Basiliximab:

A major advantage of baslliliximab is the decreased risk of infection when compared to T-cell depleting agents. According to the various studies conducted, there is no increase noted in the incidence of CMV, fungal and bacterial infections when compared to placebo or other therapies for induction [14].When basiliximab has been used for rejection there was increase in incidence of CMV infection when compared to ATG (17.5% v 7.8%) .But this is not proven in other studies. In clinical trials leading to basiliximab's approval, the overall incidence of cytomegalovirus infection was similar in basiliximab- and placebo-treated patients (15% vs. 17%) receiving a dual- or triple-immunosuppression regimen. When basiliximab is given to

patients receiving a triple-immunosuppression regimen, the cytomegalovirus infection was higher when compared to patients treated with placebo (11% vs. 5%) . The risk of infections, serious infections, and infectious organisms were same in the both basiliximab- and placebo treated patients among dual- and triple-therapy received patients.[14]

Comparison between basiliximab and antithymocyte globulin regarding infection:

A study was conducted by Christian Medical College, Vellore from January 2006 to December 2008 [15] in consecutive living related renal allograft recipients undergoing kidney transplantation between the two induction groups. One group received Basiliximab and the other received ATG. The incidence of tuberculosis (1.8, 0.0 & 7.6%: p=0.04*) and BK virus infection (0, 4.8 & 6.7%: p=0.001*) were less in the basiliximab group. The incidence of pulmonary infections, bacterial sepsis (Non UTI), systemic mycosis, CMV disease and herpes virus infections were also less in basiliximab groups . Patients who received ATG (but not basiliximab) had a higher incidence of new onset diabetes after transplantation (21.4, 38.1 & 12.4%: p=0.004[#]) and leucopenia .

A study conducted by chinese from Feb. 2007 to Jul. 2012 compared the safety between lymphocytes scavenger and IL-2 receptor blocking agent, in living kidney transplant recipients. There was no significant difference in the incidence of infection and the survival rate of patient/allograft (P>0.05) within one year after

transplantation. Both the inducing agents had reduced the incidence of acute rejection within one year but did not increase the incidence of infection.[16]

In a study conducted by Brennan DC and his colleagues in renal transplant recipients, it was concluded that patients receiving anti thymocyte globulin had a higher incidence of infection (85.8%) when compared to Basiliximab (75.2%) received patients P=0.03. But the incidence of cytomegalovirus(7.8%)is lower in ATG group compared to Basiliximab group (17.5%)[18]

In another study conducted by Carlsen J and his colleagues in cardiac transplant patients who received induction agents , it was concluded that the bacterial infections were significantly higher in ATG group than in the Daclizumab group (p=0.05)[19]

In a 6 month prospective study conducted by Mattei MF and his colleagues in cardiac transplant patients , infection death were less frequent in basiliximab group compared to ATG group (0 of 38 vs 6 of 42, p=0.027) [20]

Calcineurin inhibitors:[14]

Calcineurin inhibitors was first introduced in 1980s . It includes cyclosporine A and tacrolimus (FK506). Calcineurin inhibitors have become the major maintenance immunosuppressive drug. Tacrolimus binds to FK506-binding proteins 12 (FKBP12) and inhibits calcineurin activity and production of interleukin-2 (IL-2) needed for T cell proliferation is blocked, leading to decreased T-cell response for alloantigens. Tacrolimus is 100 times more potent than cyclosporine .

Side effects:

The side effects to tacrolimus are nephrotoxocity, hyperkalemia, hypomagnesemia posttransplant diabetes, neurotoxicity (such as headache, seizure, posterior leukoencephalopathy, and hand tremor, gastrointestinal symptoms (diarrhoea and abdominal discomfort), alopecia, hyperuricemia and exacerbation of gout occur .Close monitoring of tacrolimus levels is essential to avoid drug overdose or under dosing due to drug-drug interaction.

Infection and Tacrolimus:

Mycophenolate mofetil causes a significant increase in incidence of BK virus nephropathy in renal transplant recipients .Calcineurin inhibitors are believed to have antifungal attributes . Calcineurin is required for growth of C. neoformans at 37oC but not at 24oC. Tacrolimus demonstrated greater activities against C. neoformans than cyclosporine. Calcineurin inhibitors also have antifungal activity against A. fumigatus . Additionally, calcineurin inhibitors enhance the activities of antifungal agents.

Mycophenolate Mofetil (MMF):[14]

MMF which is one of the triple immunosuppressive drugs is a potent inhibitor of inosine-5'-monophosphate dehydrogenase. It is metabolized to mycophenolic acid . and inhibits de novo synthesis of guonosine which results in a lack of deoxyguanosine triphosphate so that DNA synthesis is suppressed . Decreased DNA synthesis leads to decreased proliferation of T and B lymphocytes .The cells affected

by MMF are the activated T lymphocytes, cytotoxic T cells, B lymphocytes, and immunoglobulin .It is used as a calcineurin inhibitors- or steroid-sparing agent.

Side effects:

Anemia or leukopenia and gastrointestinal effects(mainly diarrhoea) are most common side effects in patients receiving MMF. These symptoms are usually dose-related, and may be improved with dose reduction.

Infection and MMF:

CMV disease is the infection most commonly associated with receipt of MMF. A higher incidence of CMV disease in patients receiving MMF at a dose of either 3g/day or 2g/day was note than Azathioprine based regimen. Nevertheless, in a review and meta-analysis of calcineurin inhibitor sparing with MMF in 19 randomized controlled trials with cyclosporine as the comparator in most studies, the incidence of infections and CMV disease/infection rates did not differ in two groups . Additionally, patients receiving MMF with or without tacrolimus were more likely to have BK virus viremia or nephropathy . Varicella-zoster virus has also been reported to occur more commonly in MMF recipients.

MMF has shown antimicrobial activities against various pathogens in in vitro or animal models, including Dengue virus, hepatitis C virus, hepatitis B virus, Pneumocystis jirovecii, Coxsachie virus B3, West Nile virus, yellow fever virus, and human immunodeficiency virus (HIV). Only its activity against Pneumocystis pneumonia (PCP) in liver transplant recipients is proved clinically.

Infection in transplant recipients based on time since transplant:[33]

"Infection in transplant recipients based on time since transplant" is the idea first described by Jay A Fishman and Robert H. Rubin in their study "Infection in organ transplant recipients".

Gist of the study:

The risk of infection in solid organ transplant recipients depends primarily on two major factors

- Intensity of exposure to potential pathogens(Epidemiologic exposure)
- Combined effect of all the factors which contributes to a patient's susceptibility to infection (net state of immunosuppression)

Concept:

a)Immune status of the patient is normal- Infection has occurred

↓

Increased environmental exposure / the level of immunosuppression is greater than was thought

↓

b)Minimal environmental exposure-infection has occurred

Level of immunosuppression was high

Epidemiologic exposure:

This can occur in hospital or community which is called nosocomial or community acquired respectively. Nosocomial pathogens are mostly pseudomonas, methicillin resistant staph aureus, vancomycin resistant enterococci, candida etc. Community acquired pathogens are mostly organisms like respiratory viruses, food borne pathogens like salmonella, Listeria monocytogenes, Campylobacter jejuni, tuberculosis, dimorphic fungus etc

Net state of immunosuppression: It is due to

- Immunosuppressive therapy: dose, duration, and temporal sequence
- Underlying immune deficiency: autoimmune disease, functional immune deficits
- Integrity of the mucocutaneous barrier: catheters, epithelial surfaces
- Devitalized tissue, fluid collections
- Neutropenia, lymphopenia
- Metabolic conditions
- Uremia
- Malnutrition
- Diabetes
- Alcoholism with cirrhosis
- Infection with immunomodulating viruses

- Cytomegalovirus
- Epstein–Barr virus
- Hepatitis B and C viruses
- Human immunodeficiency virus

Time table of infection after transplant according to Rubin:

Infection in first month after transplantation:

Most of the infections which occur during the period are nosocomially acquired pathogens. Usually 90% of them are bacterial or candidal infection. Most of the infections are surgical site infections, nosocomial pneumonia, urinary tract infections or infection related to vascular access devices. the important factors determining such infections are the nature of operation, the surgical skills, duration of vascular access, drainage catheter, duration of intubation, presence of indwelling stents, foreign bodies and presence of fluid collection and devitalised tissues. Due to antimicrobial prophylaxis, the incidence is very much reduced.

Very rarely infection from the donor through the graft may get reactivated. Opportunistic pathogens such as fungal infection and CMV is very rare during this period even though the immunosuppression is maximum during this period. This is because the net state of immunosuppression is determined by the sustained level of immunosuppression the patient had rather than the dosage of the drug given during that period.

Infection one to six months after transplantation:

During this period, the residual effects of earlier infection may persist and newer infections may appear. The immunomodulatory viruses like CMV, EB virus, HBV, HCV, HIV exert the primary effect during this period. These infections along with sustained immunosuppression leads to patient's net state of immunosuppression leading to opportunistic infections like mycelial fungal infections, Pneumocystis carinii ,dimorphic fungii etc.

More than 6 months after transplantation:

Three types of patients

Type 1: 80% patients have good allograft functions. Low level of immunosuppression received. Infections are similar to common people.

Type 2 : 10% patients have chronic infection with HBV, HCV, CMV, EBV or have diabetes ,malignancy which may increase the risk of infection leading to secondary infections .

Type 3 : 5-10% patients have recurrent rejection requiring increased immunosupprression which results in opportunistic infections.

MATERIALS & METHODS

Type of study:

Both prospective and retrospective study

Place of Study & Period of Study:

Department of Microbiology, Stanley Medical college,

Department of Nephrology, Stanley Medical college.

Study period:

September 2014 to August 2015.

Sample size and Inclusion criteria:

A total of 147 post renal transplant recipients who are followed as inpatients and outpatients in the Department of Nephrology, Stanley Medical College were taken for the study. The details of lower respiratory tract infection that occurred previously is collected from the patient's record and the newer samples were also collected and processed from the patients with symptoms and signs of respiratory tract infection .

Ethical Consideration

Ethical and research clearance was obtained from the Ethical committee, Stanley Medical College. Permission to conduct the study was sought from the respective hospital department authorities. Informed consent was obtained from the patients before enrolment in to the study.

Statistical Analysis

The collected data was analyzed with SPSS 21.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and S.D were used. To find the significance in categorical data Chi-Square test was used. The probability value 0.05 is considered as significant level. To test the significance between two proportions, z test for proportion is used.

SPECIMEN COLLECTION AND LABORATORY TESTING:

After obtaining proper history and consent, samples were collected from post renal transplant patients with suspected lower respiratory tract infections.

Expectorated sputum:

The patient was educated about the difference between sputum and oral secretions. The patient was asked to rinse the mouth with distilled water or normal saline (sterile) and then expectorate deep cough sputum directly into a sterile screw-cap collection cup or sterile dry container. The patient was instructed not to expectorate saliva or post nasal discharge into the container.

Induced sputum:

Using a wet tooth brush and sterile water or saline the patient was instructed to brush the buccal mucosa, tongue, and gums for 5 to 10 minutes prior to the procedure. Tooth paste should not be used. Patient was asked to rinse the mouth with sterile water or saline. Using an ultrasonic nebuliser, the patient was asked to inhale 20-30 ml of 3% NaCl. The induced sputum was collected in a sterile leak proof container.

Bronchoalveolar washing or BAL sample:

The BAL sample was obtained from the distal respiratory bronchioles and alveoli. Bronchial washings sample was obtained from the major airways.

The bronchoscope was passed transorally or transnasally. Inject sterile nonbacteriostatic 0.85% NaCl from a syringe through a biopsy channel of the bronchoscope. BAL sample was collected wedging the tip of bronchoscope into an airway lumen and instilling a large volume of sterile, nonbacteriostatic saline. The sample obtained contains secretions distal to the bronchioles and alveoli. The recovered specimen is suctioned into a sterile container.

Transbronchial biopsy samples:

Biopsy sample was obtained through the biopsy channel of the bronchoscope and transport in a sterile container with a small amount of non bacteriostatic saline.

Specimen transport:

The collected lower respiratory tract specimen was transported immediately to the laboratory and processed according to the standard microbiological procedure.

Blood collection:

About 12 ml of whole blood was collected by venepuncture by strict aseptic technique . About 8ml of the blood was inoculated into biphasic broth (Trypticase soy agar with Brain heart infusion agar). 4ml of the blood was kept for pp65 antigen detection of CMV.

Viral Studies:

PP65 antigen in polymorphonuclear leukocytes from peripheral blood for CMV was done by giving the sample to outside laboratory.

Processing of lower respiratory tract samples was done as below

Direct smear with gram's staining:

The thick purulent part of the sputum was taken and smeared on to a clean glass slide about 2cm in breath and 1cm in width. The smear was then air dried and heat fixed and was stained by gram staining technique.

The smear was mounted on the oil immersion microscope and was looked for the presence of pus cells and bacteria and epithelial cells .

AFB staining:

The sputum obtained was first concentrated by modified Petroff's method by digestion and decontamination. Digestion was done by N- Acetyl-L-Cysteine (NALC) and decontamination was done by 2% NaOH.

Digestion and decontamination procedure:

Preparation of N-Acetyl cysteine and alkali mixture:

50 ml of 2.94% trisodium citrate-3.H2O (0.1 M) was mixed with 50 ml of 4% NaOH. Then 0.5g of NALC powder was added to this mixture. NALC was a mucolytic agent. It does not have any bacteriocidal activity. It liquefies the mucus by splitting the disulphide bridges. The mycobacteria are released from the mucus plug on liquefaction.

A 50ml of plastic centrifuge was taken and equal volume of NALC and alkali mixture is added to equal volume of the specimen. The screw cap is tightened. The mixture is homogenised with a vortex mixer for 15- 20 seconds. Then the tube is

allowed to stand for 20 minutes at room temperature. The digestion time should not exceed 20 minutes.

After 20 minutes, phosphate buffer(pH 6.8) was added up to the ring in the top of the centrifuge tube and is mixed well. The specimen was centrifuged at 2000g for 15-20 minutes. After centrifugation, the supernatant was discarded into a splash proof container containing phenolic disinfectant. A small quantity of phosphate buffer was added and the sediment was resuspended with a Pasteur pipette.

Kinyoun's method of Acid fast staining:

A portion of the sediment was smeared on to a clean glass slide about 2cm length and 1 cm breath with a sterile bacteriological loop or an applicator. The smear was air dried and heat fixed.

Culture is onto Lowenstein and Jensen medium:

A portion of the sediment was streaked onto one two bottles of LJ medium for the culture of Mycobacterium species and was maintained for eight weeks.

KOH mount:

A clean dry slide was take and a drop of KOH was placed on the slide . A loop full of sputum was placed over the KOH and mixed well . A cover slip was placed over the sputum and left for 2 minutes at room temperature. Then the slide was mounted on low power and in high power for the presence of hyphal and other fungal elements.

Culture onto bacterial culture media:

The sputum was cultured onto blood agar, chocolate agar and MacConkey medium and incubated overnight at 37◦C. The next day the plates are looked for the appearance of colony morphology, haemolysis, pigmentation, whether lactose or non lactose fermenter. Then smear was done from the colonies on culture plate and examined under oil immersion microscope. According to the smear results, biochemical tests are done appropriately to find out the bacterial organisms and antibiotic sensitivity tests are done by Kirby Bauer method.

Kirby bauer method:

Inoculum preparation

Inoculum was prepared by direct colony suspension method by taking four to five well isolated colonies from 18-24 hours culture, in Mueller Hinton broth to achieve a turbid suspension.

Inoculum standardization

The inoculum suspension was compared with 0.5 McFarlands standard suspension by positioning the tube side by side against a white card containing several horizontal black lines. The turbidity was compared by looking at the black lines through the suspensions. Once standardized, the inoculum suspension was used within 15 minutes of preparation.

Procedure

After standardization of bacterial suspension, the suspension was vortexed to make sure, it was well-mixed. Then by using a sterile swab, inoculation was done on MacConkey agar and excess fluid was removed by pressing the swab against the side of the test-tube .Swab was streaked evenly over the surface of the medium in three directions; the plate was rotated approximately 60° for even distribution. With the petridish lid in place, three to five minutes was allowed for the surface of the agar to dry. Using sterile needle mounted in a holder, the appropriate discs were evenly distributed on the inoculated plate. The discs were placed about 15mm from the edge of the plate and not closer than about 25mm from disc to disc. Only six discs were applied on a 90mm plate. Each disc was lightly pressed down to ensure its contact with the agar. The plate was inverted and incubated at 35°C aerobically for full 24 hours.

Interpretation of results:

After incubation, the inhibition zone was measured to the nearest millimeter using a ruler, under transmitted light. Inhibitory zone includes the diameter of the disc. After measuring, the millimeter reading for each antimicrobial agent was compared with that in the interpretive tables of he CLSI guidelines and results were interpreted as either susceptible, intermediate or resistant.

Culture onto fungal culture media:

The sputum was streaked onto Sabourard's dextrose agar (two tubes) and Potato dextrose agar (two tubes)for the growth of any fungus if present and was maintained for eight weeks. One of the two tubes of each medium was maintained at

37◦C for the growth of yeast and the other tube was maintained at 25◦C for the growth of hyphal forms.

OBSERVATION & RESULTS

Total post renal transplant recipient cases followed = 147

Total Lower respiratory tract infected patients = 40

MICROBIOLOGY PROFILE OF THE LOWER RESPIRATORY TRACT INFECTED TRANSPLANT PATIENTS:

TYPE OF SAMPLES : (n=40)

Table 1

Type of sample	Frequency
Sputum	28
Bronchoalveolar lavage	9
Lung biopsy specimen	3
Total	40

CULTURE RESULTS:

Table 2

	Positive	**Negative**
Bacterial culture	16	24
Fungal culture	5	25
Culture on LJ medium	12	28

BACTERIAL ORGANISMS ISOLATED:

Table 3

GRAM POSITIVE COCCI	**2**
GRAM NEGATIVE BACILLI	**14**

Table 4

ORGANISMS	**COUNT**
Pseudomonas aeruginosa	6
Klebsiella spp	4
Staphylococcus aureus	2
Haemophillus influenza	1
Acinetobacter spp	1
Escherischia coli	1
Citrobacter spp	1

Total	16

Pseudomonas aeruginosa was the common bacterial organism isolated followed by Klebsiella spp. Gram negative organisms were more common than gram positive organisms.

FUNGUS IDENTIFICATION:

Total fungus identified=5

Table 5

KOH positive	2
Fungal culture positive	5
Biopsy suggestive	2

FUNGAL SPECIES IDENTIFIED:

Table 6

Mucor spp	2
Aspergillus fumigatus	2
Aspergillus nidulans	1

MYCOBACTERIAL IDENTIFICATION:

Total Mycobacteria identified=12

Table 7

	POSITIVE	NEGATIVE
ACID FAST STAINING	**10**	**2**
CULTURE ON LJ MEDIUM	**12**	**0**

ORGANISMS ISOLATED TIME SINCE TRANSPLANT:

Immediate postoperative period:

Table 8

ORGANISM	COUNT	SPECIFIC RESISTANCE PATTERN
BACTERIA		
Pseudomonas spp	1	AMP C PRODUCER
Acinetobacter spp	1	CARBAPENAMASE PRODUCER
Staphylococcus aureus	1	METHICILLIN RESISTANCE

Mostly multidrug resistant organisms are isolated.

<2 months:

Table 9

ORGANISM	COUNT
BACTERIA	
Pseudomonas spp	2
Klebsiella spp	1
FUNGUS	
Aspergillus	1

>2 months to 2years:

Table 10

ORGANISM	COUNT
BACTERIA	
Pseudomonas spp	2
Klebsiella spp	3
Escherichia coli	1
Citrobacter spp	1
Haemophillus spp	1
Mycobac. tuberculosis	6
FUNGUS	
Aspergillus spp	2
Mucor spp	1

Community acquired organisms and opportunistic fungal organisms were isolated

>2 years:

Table 11

ORGANISM	NO
BACTERIA	
Pseudomonas	1
Staphylococcus aureus	1
Mycobac. tuberculosis	**6**
FUNGUS	
Mucor spp	1
CMV	**1**

RESISTANCE PATTERN:

Table 12

	ORGANISMS	**TOT**	**COT**		**AK**		**CIP**		**CEF-3RDG**		**CEFOX**		**CARB**	
			S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Non Fermenter GNBS	Pseudomonas aeruginosa	6		**IR**	**5**	**1**	**3**	**3**	**5**	**1**	**5**	**1**	**6**	**0**
	Acinetobacter spp	1	**0**	**1**	**0**	**1**	**0**	**1**	**0**	**1**	**-**	**-**	**0**	**1**
Enterobactericae	Klebsiella spp	4	**0**	**4**	**4**	**3**	**2**	**2**	**2**	**2**	**-**	**-**	**4**	**0**
	Escherischia coli	1	**0**	**0**	**1**	**0**	**1**	**0**	**1**	**0**	**-**	**-**	**-**	**-**
	Citrobacter spp	1	**0**	**1**	**1**	**0**	**1**	**0**	**1**	**0**	**-**	**-**	**-**	**-**
Other GNBs	Haemophilus influenza	1	**0**	**1**	**1**	**0**	**1**	**0**	**1**	**0**	**-**	**-**	**-**	**-**

GPCs	Staphylococcus aureus	2	**0**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**-**	**-**

IR=INTRINSIC RESISTANCE R=RESISTANCE S=SENSITIVE

COT=COTRIMOXAZOLE AK=AMIKACIN CEFOX=CEFOXITIN

CEF 3RD= 3RD GENERATION CEPHALOSPORIN CIP=CIPROFLOXACIN

CARB=CARBAPENAMASE

SPECIFIC RESISTANCE PATTERN:

Table 13

SPECIFIC RESISTANCE	**NO**
Amp C Pseudomonas	1
ESBL Klebsiella spp	2
Carbapenamase producing Acinetobacter	1
MRSA	1

PATIENT PROFILE:

A total of 147 post transplant cases were studied .

Out of which males=87 and females=60.

Based on the donor type, live related transplant recipients =73, deceased donor/cadaveric transplant recipients =58. Spousal transplant recipients=16.

A total of 20 patients had received Basiliximab , 9 patients had received ATG, 35 patients were diabetes.

40 had lower respiratory tract infection.

Among the lower respiratory tract infected patients, 7 had received Basiliximab, 4 had received ATG, 9 had received intravenous pulse methyl prednisolone for rejection episodes , 11 were diabetic, 8 had Tacrolimus level >8ng/ml, 3 had HCV.

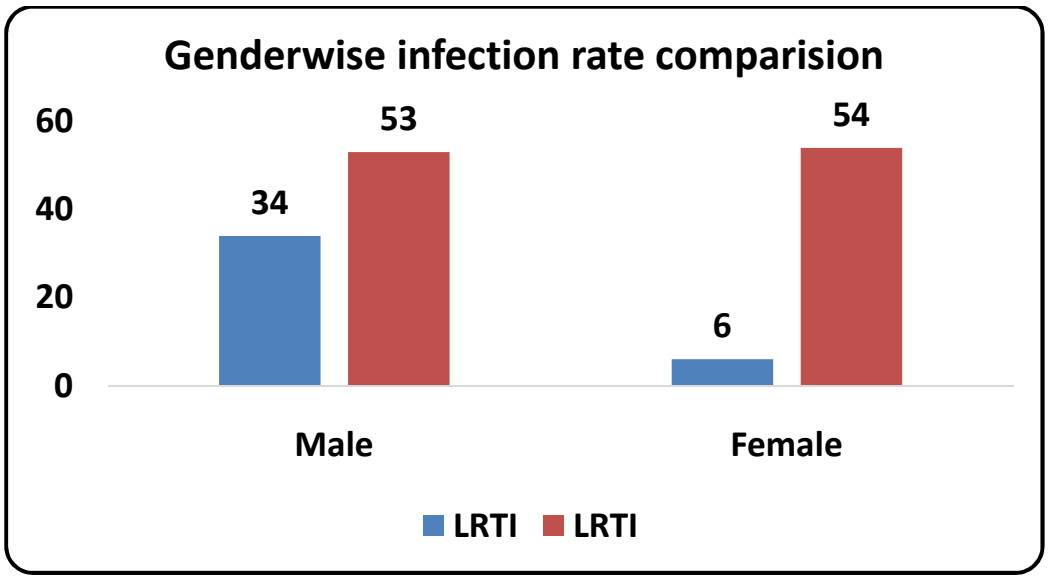
GENDER DIFFERENCE IN LOWER RESPIRATORY TRACT INFECTION AMONG TRANSPLANT RECIPIENTS:

Table 14

GENDER	LRTI		TOTAL	P-VALUE
	YES	NO		
MALE	34(39.08%)	53(60.92%)	87	
FEMALE	6(10%)	54(90%)	60	<0.001
TOTAL	40(27.21%)	107(72.79%)	147	

Prevalence of lower respiratory tract infection in renal transplant recipients is about 27.2%. The lower respiratory tract infection is more common in males (39.08%) compared to females(10%). The difference between the occurrence of lower respiratory tract infection is statistically significant (P=<0.001)

Figure 1



AGE DISTRIBUTION OF THE LOWER RESPIRATORY TRACT INFECTION PATIENTS:

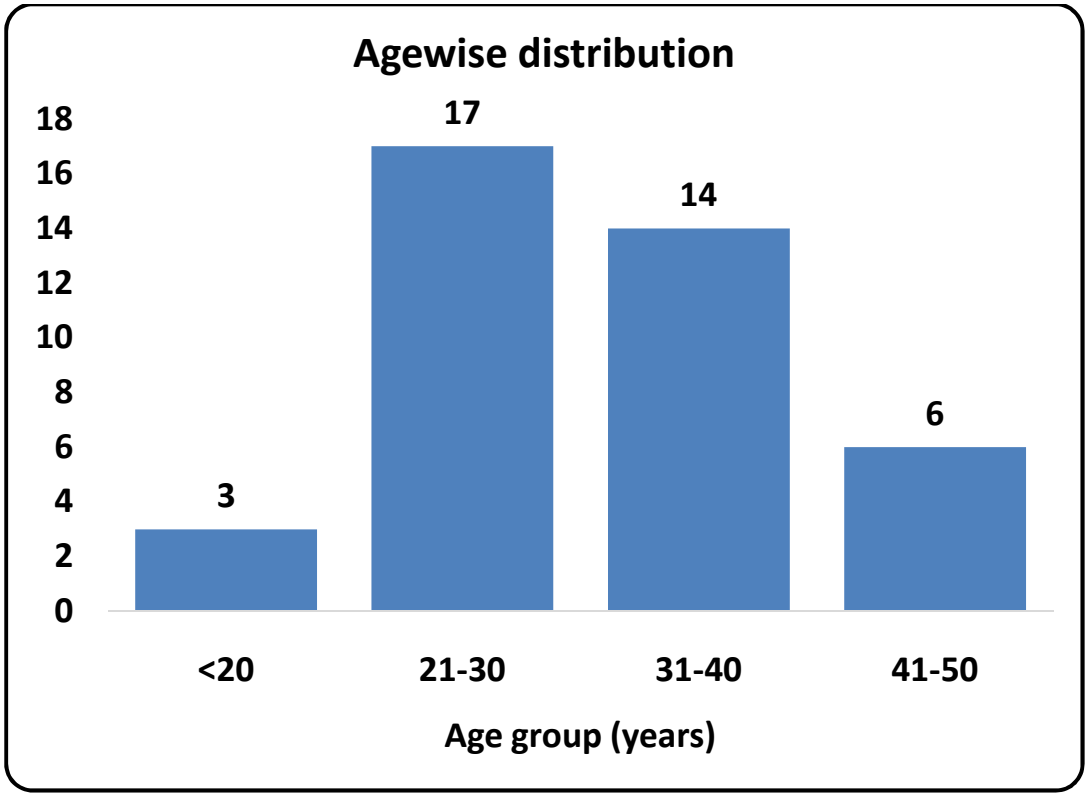
Table 15

AGE INTERVAL	TOTAL LRTI PATIENTS	RATE
10-20	3	7.5%
21-30	17	42.5%
31-40	14	35%
41-50	6	15%

MEAN AGE=32

LRTI is more common in the age group between 21-40 (77.5%)

Figure 2



LOWER RESPIRATORY TRACT INFECTION RATE AMONG TOTAL RENAL TRANSPLANT RECIPIENTS BASED ON DONOR TYPE:

Table 16

DONOR TYPE	LRTI		TOTAL	P-VALUE
	YES	NO		
LIVE RELATED	23(31.51%)	50(68.49%)	73	0.33
SPOUSAL	2(12.5%)	14(87.5%)	16	
CADAVER	15(25.86%)	43(74.14%)	58	
TOTAL	40(27.21%)	107(72.79%)	147	

Percentage of infections more common in live related donor transplant recipients (31.5%) compared to deceased donor transplants recipients(25.8%). There is no statistical significance in the occurrence of lower respiratory infection between the two (P=0.33)

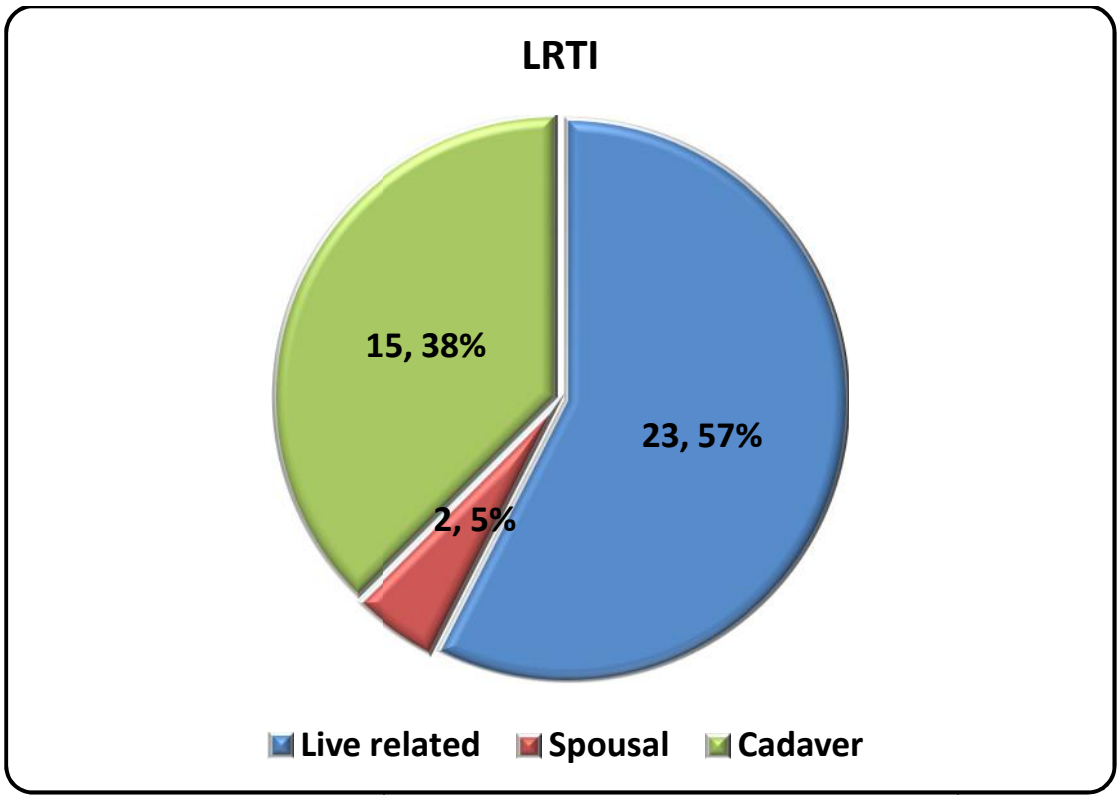
INFECTION RATE AMONG LOWER RESPIRATORY TRACT INFECTION PATIENTS BASED ON DONOR TYPE:

Table 17

DONOR TYPE	NO. OF INFECTED	RATE
LIVE RELATED	23	57.5%
SPOUSAL	2	5%
CADAVER	15	37.5%

Among the lower respiratory infection patients , the highest occurrence is in live related transplants (57.5%) compared to deceased donor transplant(37.5%)

Figure 3



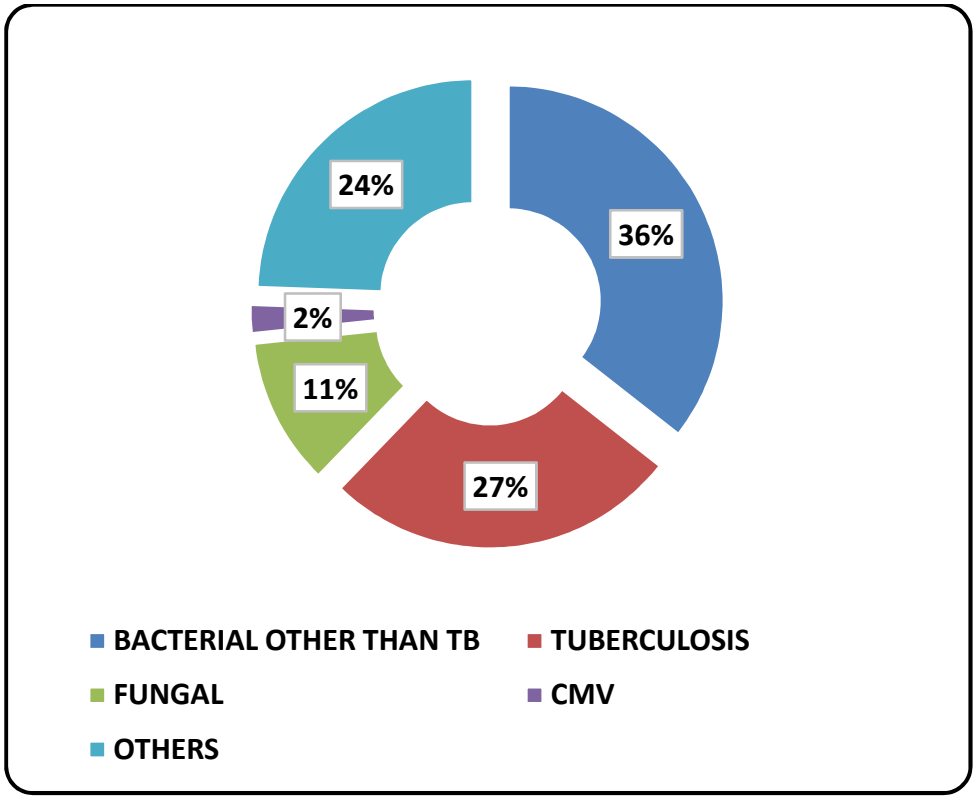
TYPES OF INFECTION AMONG THE RESPIRATORY TRACT INFECTION PATIENTS:

Table 18

TYPES OF INFECTION	NO. OF INFECTION	RATE AMONG TOTAL ORGANISMS
BACTERIAL OTHER THAN TB	16	35.55%
TUBERCULOSIS	12	26.66%
FUNGAL	5	11.11%
CMV	1	2.22%
OTHERS	11	24.44%

Among the organisms isolated , the highest is bacterial infection(35.55%) followed by tuberculosis(26.66%), fungi (11.11%) respectively. In 24.44% of the patients, no organisms were isolated.

Figure 4



ORGANISM SPECIFIC INFECTION RATE :

Table 19

ORGANISMS	NO.OF PATIENTS	RATE AMONG LRTI	RATE AMONG TOT PTS
TB	12	30%	8.1%
FUNG.PNE	5	12.5%	3.4%
BACTER PNEUM	16	40%	10.8%
CMV	1	2.5%	0.68%

Among the 40 LRTI patients, bacterial pneumonia contributes to about 40%, tuberculosis contributes about 30% of the infection and fungus contributes about 12.55% of the infection.

Among the total renal transplants, the rate of bacterial pneumonia is 10.8%, the rate of pulmonary tuberculosis is 8.16%, the rate of fungal pneumonia is 3.4% and CMV is 0.68%

Figure 5

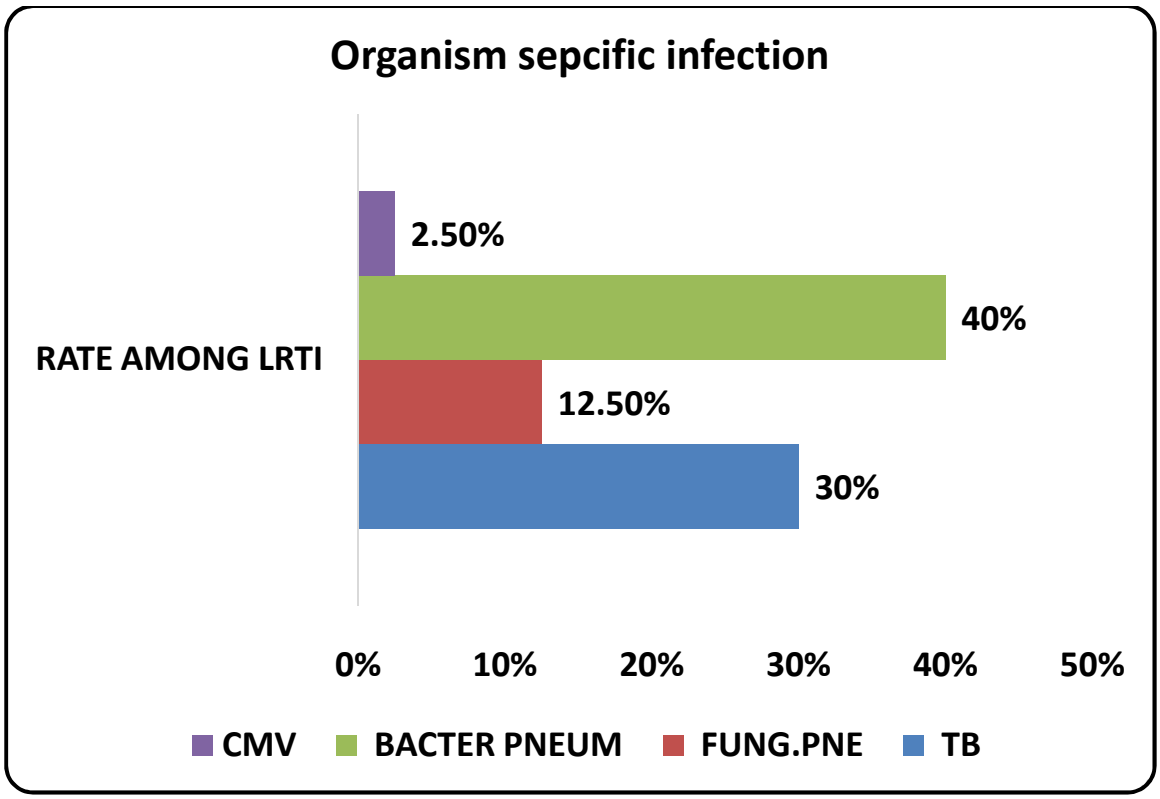
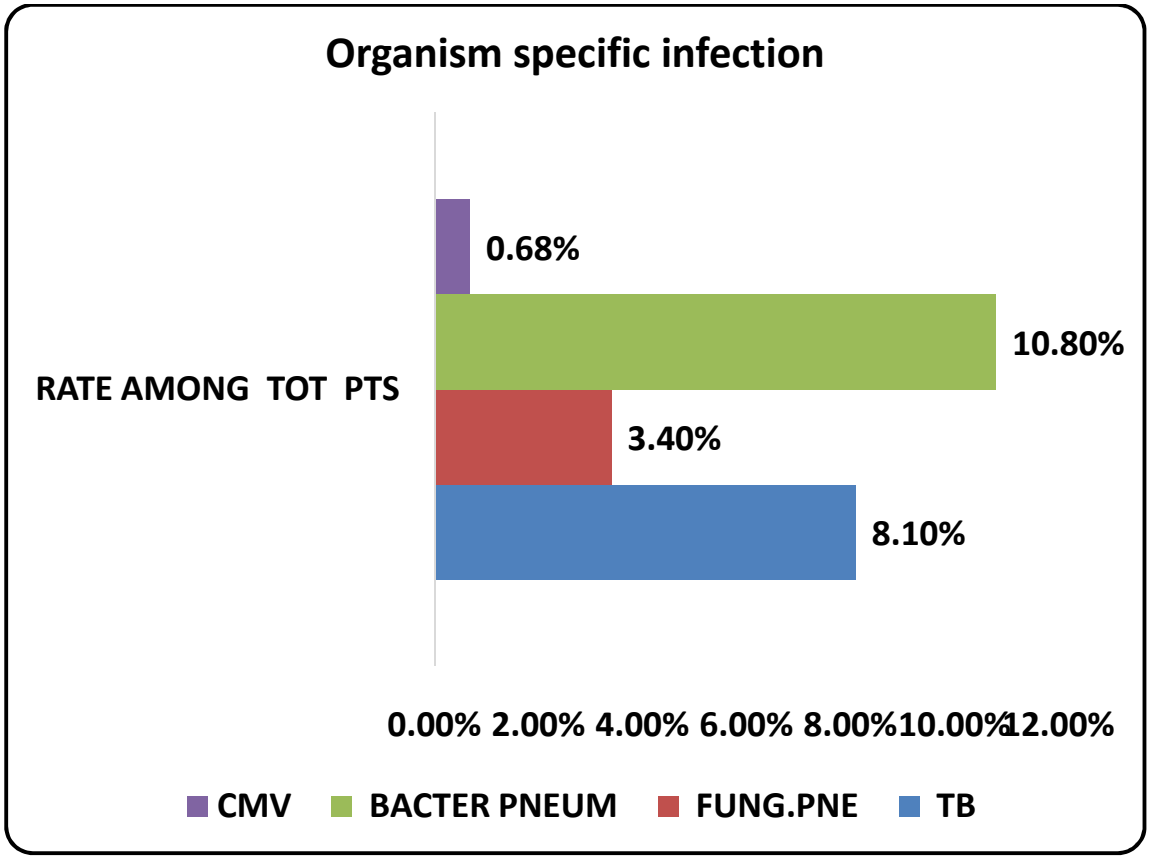

Organism sepcific infection
RATE AMONG LRTI
2.50%
40%
12.50%
30%
0%
10%
20%
30%
40%
50%
CMV
BACTER PNEUM
FUNG.PNE
TB

Figure 6


Organism specific infection
RATE AMONG TOT PTS
0.68%
10.80%
3.40%
8.10%
0.00%
2.00%
4.00%
6.00%
8.00%
10.00%
12.00%
CMV
BACTER PNEUM
FUNG.PNE
TB

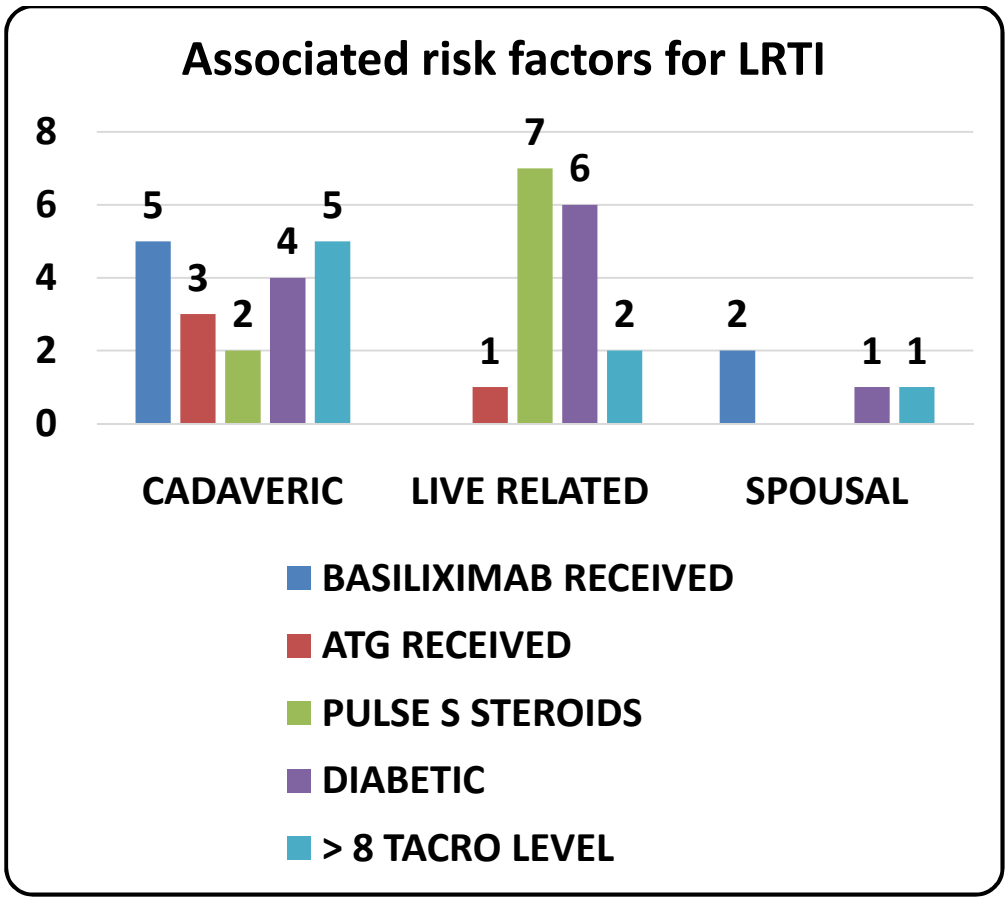
RISK FACTORS FOR INFECTION ASSOCIATED WITH LOWER RESPIRATORY TRACT INFECTED TRANSPLANTS:

Table 20

RISK FACTORS	CADAVERIC	LIVE RELATED	SPOUSAL
BASILIXIMAB RECEIVED	5	-	2
ATG RECEIVED	3	1	-
PULSE S STEROIDS	2	7	-
DIABETIC	4	6	1
> 8 TACRO LEVEL	5	2	1

Cadaveric transplant recipients are associated with more risk factors than live related transplants. But pulse steroids are more in live related transplants.

Figure 7

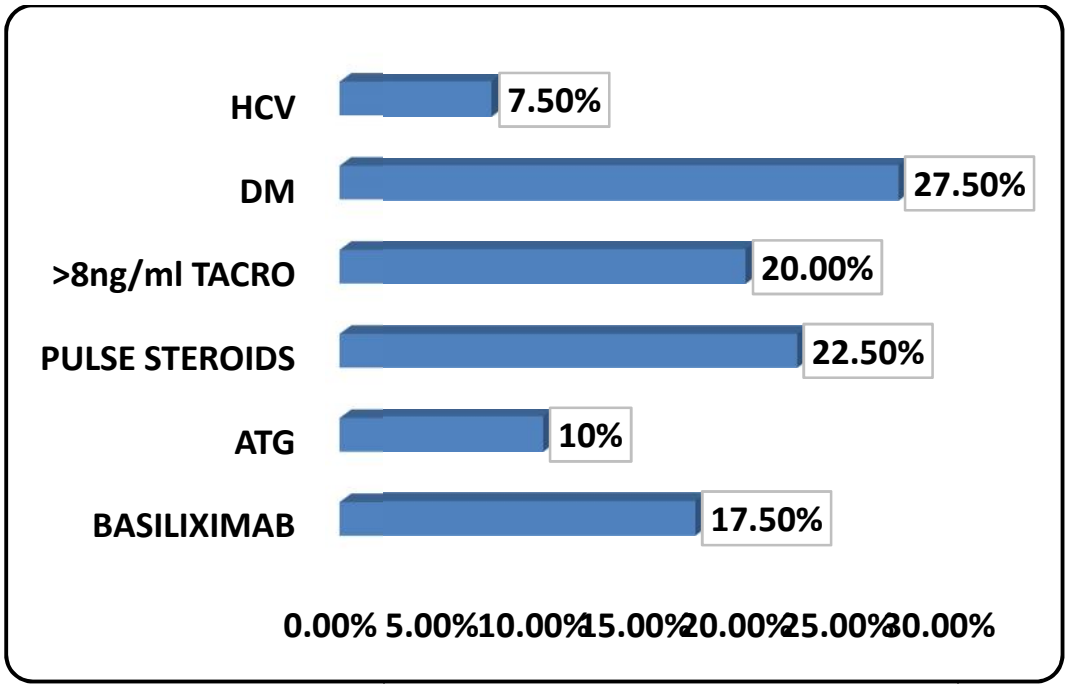


INDIVIDUAL RISK FACTORS FOR LOWER RESPIRATORY TRACT INFECTION IN RENAL TANSPLANT RECIPIENTS:

Table 22

RISK FACTORS	LRTI PTS N(%)
BASILIXIMAB	7(17.5%)
ATG	4(10%)
PULSE STEROIDS	9(22.5%)
>8NG/ML TACRO	8(20%)
DM	11(27.5%)
HCV	3(7.5%)

Diabetes (27.5%) is the leading risk factor associated with lower respiratory tract infection patients (27.5%) , followed by pulse steroids (22.5%) which is given for rejection.



ORGANISM SPECIFIC INFECTION RATE AMONG LOWER RESPIRATORY TRACT INFECTED PATIENTS WITH RISK FACTORS:

Table 23

ORGANISMS	ATG (N=4)	BASILI (N=7)	PULSE (N=9)	DIABETIC (N=11)	>8 ng/ml TACRO (N=8)	HCV (N=3)
TB RATE	2(50%) [a]	-	4(44.44%) [a]	4(36.36%) [a]	1(12.5%) [a]	1(33.33 %) [a]
FUNG.PNEUMO RATE	-	2(28.57%) [a]	1(11.11%) [a]	4(36.36%) [*]	1(12.5%) [a]	1(33.33 %) [a]
BAC.PNEUMO RATE	1(25%) [a]	3(42.8%) [a]	6(66.66%) [*]	3(27.27%) [a]	4(50%) [a]	-
CMV	-	-	-	1(9.09%) [a]	-	-

[a]= P>0.05, *=P<0.05

In the association of specific risk factors with specific infection by proportion test, only pulse steroids has statistical significance with bacterial pneumonia (P=0.03) and diabetes has statistical significance with fungal pneumonia (P=0.002) and others are not.

LOWER RESPIRATORY TRACT INFECTION RATE AMONG RENAL TRANSPLANT RECIPIENTS WHO RECEIVED INDUCTION AGENTS:

Table 24

INDUCTION AGENTS	BASILIXIMAB	ATG	P-VALUE
TOTAL CASES FOLLOWED	20	9	0.68
TOTAL LRTI	7(P=0.8)	4(P=0.88)	
LRTI RATE	35%	44.44%	

The rate of lower respiratory tract infection occurred is more in ATG (44.44%) than basiliximab (35%) but there is no statistical significance between the two (P=0.68). Basiliximab (P=0.8) and ATG (P=0.88) has no statistical significance with lower respiratory tract infection in renal transplant recipient patients.

ORGANISM SPECIFIC INFECTION RATE AMONG TOTAL DIABETIC TRANSPLANT RECIPIENTS:

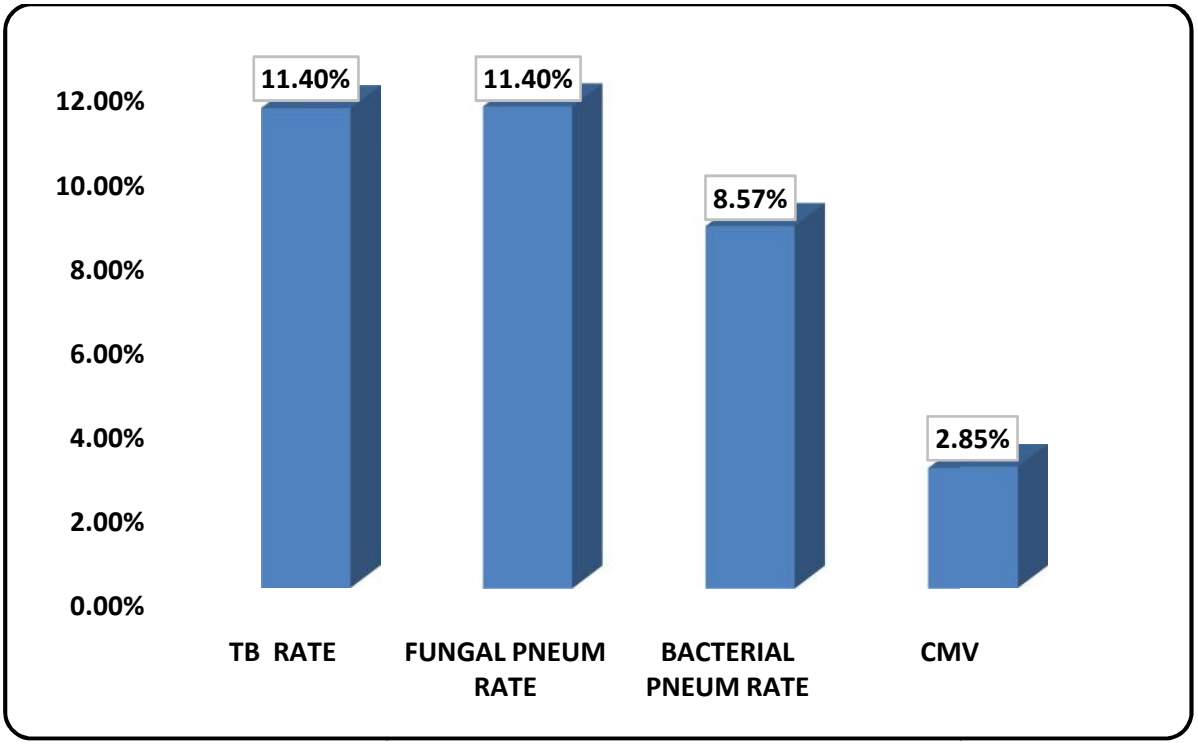
TOTAL DIABETICS AMONG THE PATIENTS WITH RESPIRATORY TRACT INFECTION= 11/40

Table 25

ORGANISM	NO.OF DIABETIC PATIENTS (N=35)
TB RATE	4(11.4%)
FUNGAL PNEUM RATE	4(11.4%)
BACTERIAL PNEUM RATE	3(8.57%)
CMV	1(2.85%)

The rate of lower respiratory tract infection has no statistical significance with diabetes.(P=0.73). But fungal pneumonia has statistical significance with Diabetes (P=0.002)

Figure 8



ORGANISM SPECIFIC INFECTION RATE AMONG DIABETIC LRTI PTS:

Table 26

ORGANISMS	HYPERGLYCEMIA UNDER CONTROL	UNCONTROLLED HYPERGLYCEMIA	RATE
TB RATE	60%	16.66%	36.36%
FUNGAL PNEUM RATE	20%	66.66%	45.45%
BACTERIAL PNEUM RATE	20%	33.33%	27.27%
CMV	0%	16.66%	9.09%

Fungal pneumonia (66.66%) and bacterial pneumonia (33.33%) is more common in poorly controlled diabetes patients.
HCV with pulmonary TB= 8.33%
Fungus pneumonia in pulmnary TB patients= 8.33%

PART OF THE LUNG LOBES AFFECTED AMONG TUBERCULOSIS AND FUNGAL PNEUMONIA:

Table 27

LOBE AFFECTED	TB	RATE	FUNGUS	RATE
UPPER LOBE/ APICAL	7	58.33%	4	80%
MIDDLE LOBE	1	8.33%	0	0%
LOWER LOBE	3	25%	1	20%
PEURAL EFFUSION	2	16.66%		
MEDIASTINAL LYMPHADENOPATHY	1	8.33%		

In both the fungal pneumonia (80%) and pulmonary tuberculosis (58.33), upper lobe of the lung is most commonly affected.

TYPE OF FUNGUS ISOLATED:

Table 26

FUNGUS	NO OF PATIENTS	RATE	MORTALITY RATE
MUCOR	2	40%	0%
ASPERGILLUS	3	60%	66.66%

FUNGUS WITH BACTERIAL INFECTION=2/5

TB+ FUNGUS= 1/5

Aspergillus and mucor are the species causing fungal pneumonia. The mortality rate is 66.66%

>8NG/ML TACROLIMUS LEVEL AND SPECTRUM OF ORGANISMS

TOTAL LRTI PATIENTS ON TACROLIMUS=35

TACRO LEVEL KNOWN=32 PTS

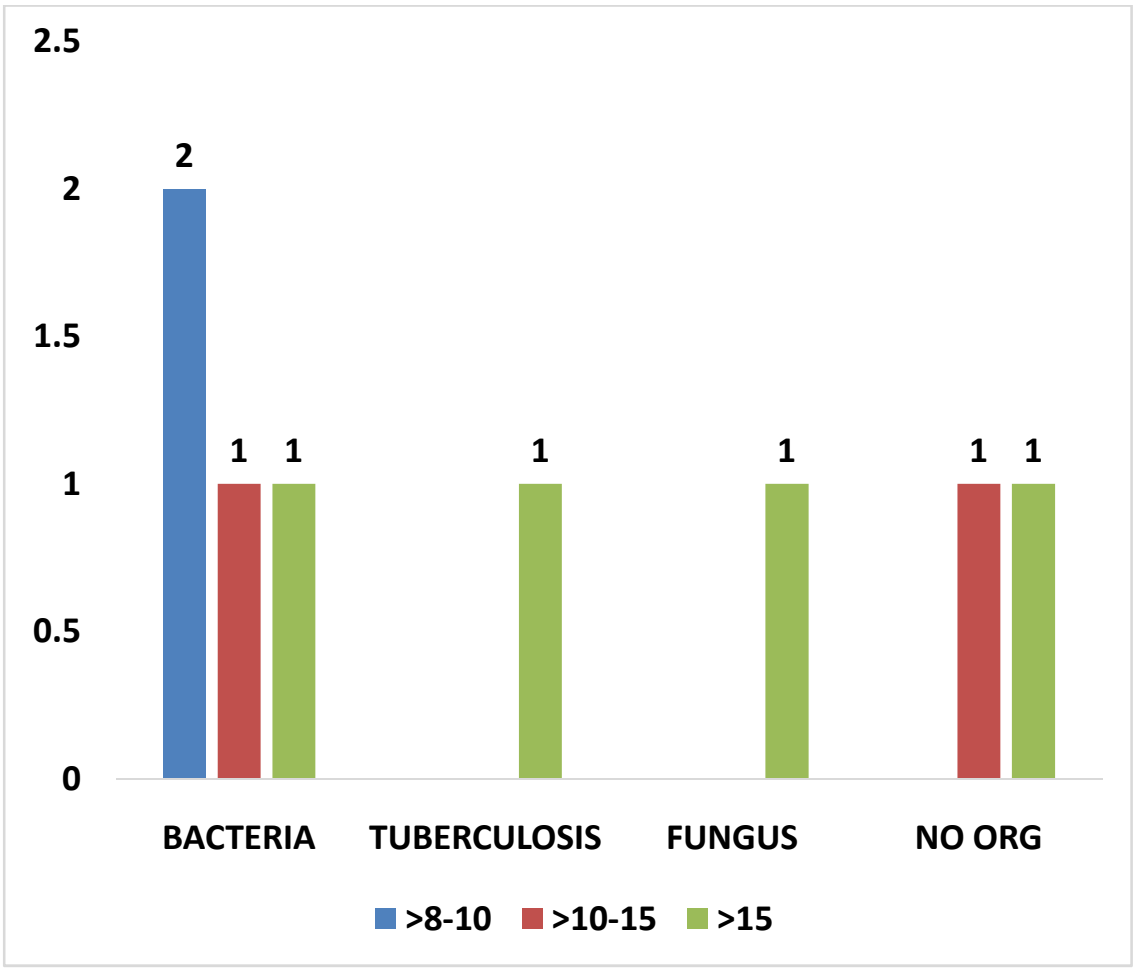
Table 27

TACRO LEVEL	BACTERIA	TUBERCULOSIS	FUNGUS	NO ORG	TOTAL
>8-10	2	0	0	0	2
>10-15	1	0	0	1	2
>15	1	1	1	1	3

7 patients had tacrolimus level more than 8ng/ml in our study.

>8NG/ML TACROLIMUS LEVEL AND SPECTRUM OF ORGANISMS

Figure 9



INFECTION RATE AMONG LOWER RESPIRATORY TRACT INFECTION PATIENTS BASED ON TIME SINCE TRANSPLANT:

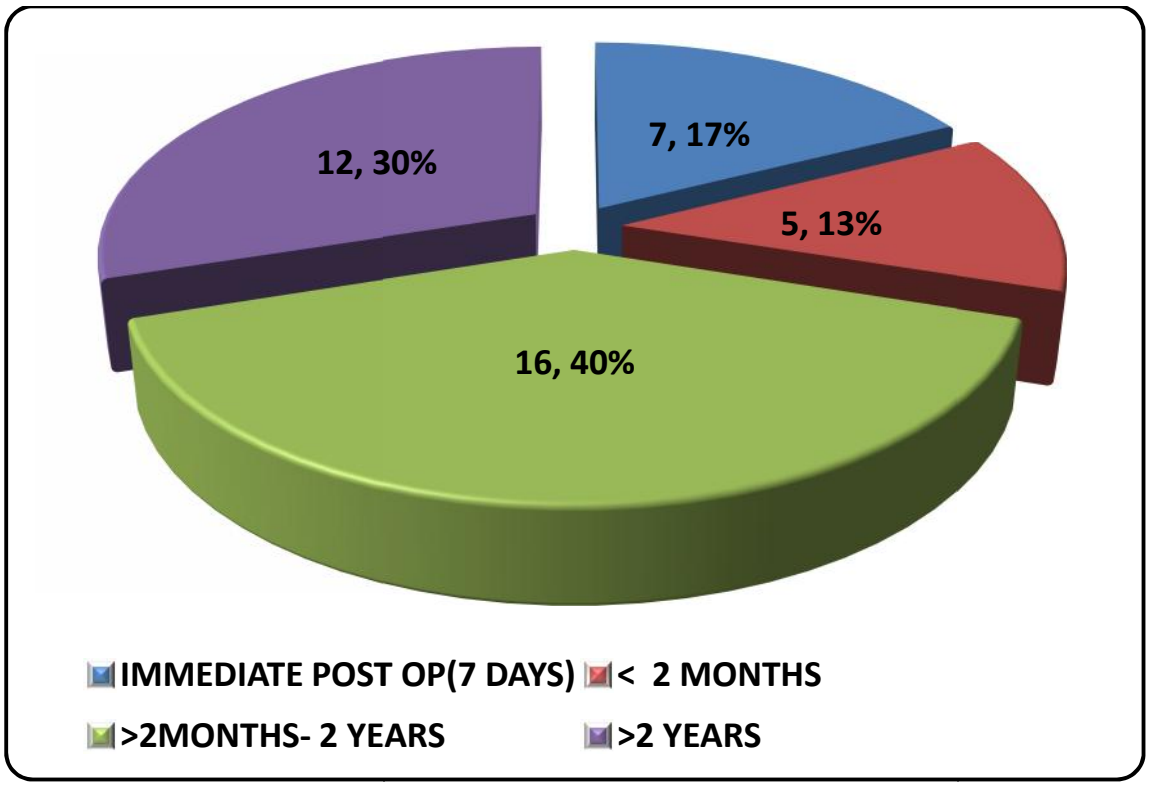
TOTAL CASES=40

Table 28

TIME SINCE TRANSPLANT	NO OF CASES	INFECTION RATE
IMMEDIATE POST OP(7 DAYS)	7	17.5%
< 2 MONTHS	5	12.5%
>2MONTHS- 2 YEARS	16	40%
>2 YEARS	12	30%

The highest rate of LRTI occurs in the period between >2months-2years (40%) followed by >2 years (30%) post transplant.

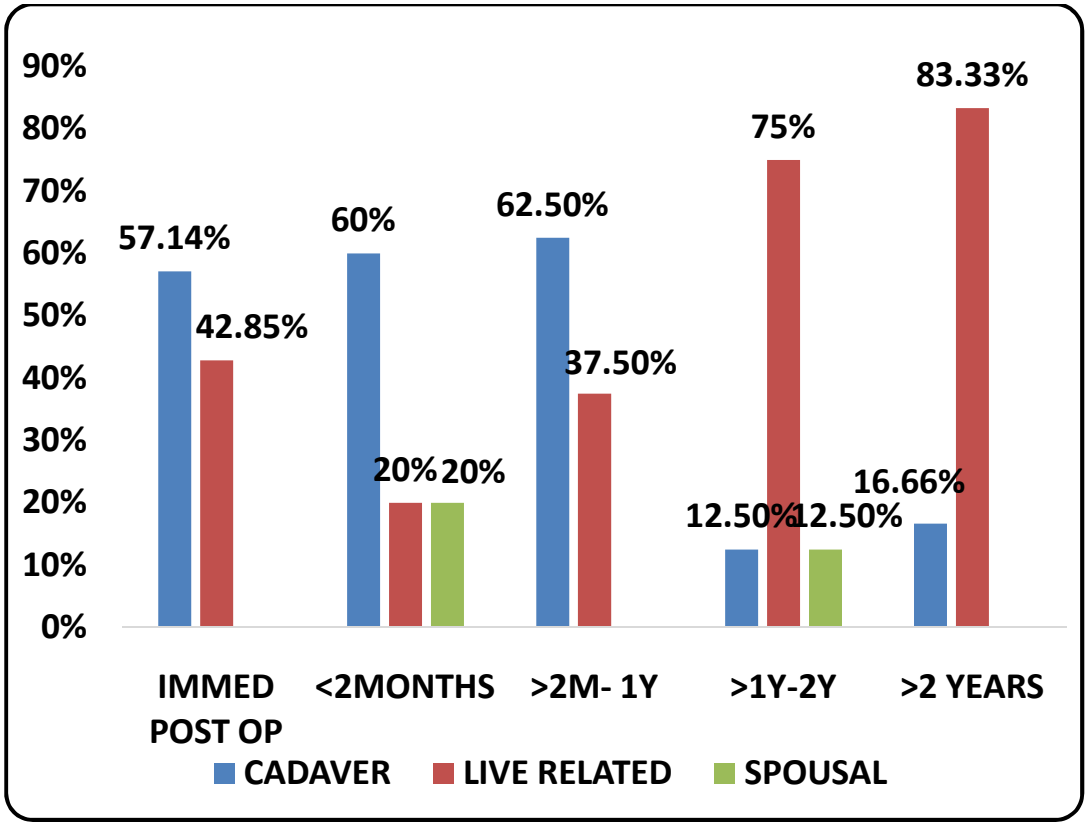
Figure 10



OCCURENCE OF LOWER RESPIRATORY TRACT INFECTION TIME SINCE TRANSPLANT BASED ON DONOR TYPE:

Table 29

DONOR TYPE	IMMED POST OP	<2MONTHS	>2MONTHS-2YEARS		>2 YEARS
			>2M- 1Y	>1Y-2Y	
CADAVER	57.14%	60%	62.5%	12.5%	16.66%
LIVE RELATED	42.85%	20%	37.5%	75%	83.33%
SPOUSAL	0	20%	0	12.5%	0



Up to 1 year time since transplant, lower respiratory infection is more common in cadaveric transplant recipients (60%). After 1 year , it is common in live related transplant recipients (80%).

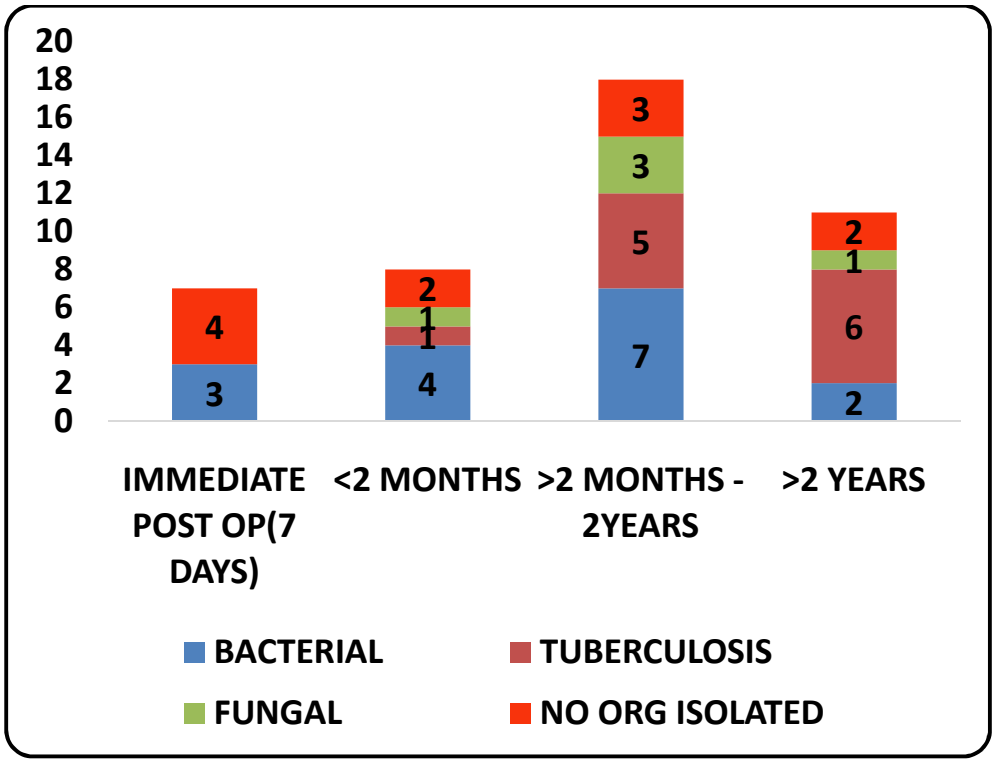
SPECTRUM OF ORGANISMS CAUSING LOWER RESPIRATORY TRACT INFECTION TIME SINCE TRANSPLANT :

Table 30

INTERVAL	BACTERIAL	TUBERCULOSIS	FUNGAL	NO ORG ISOLATED
IMMEDIATE POST OP(7 DAYS)	3	0	0	4
<2 MONTHS	4	1	1	2
>2 MONTHS - 2YEARS	7	5	3	3
>2 YEARS	2	6	1	2
TOTAL PTS	16	12	5	11

Bacterial pneumonia peaks in the period of <2 months time since transplant whereas tuberculosis and fungus pneumonia is commonly found in the period of >2 months to 2 years.

Figure 12



RISK FACTORS AND OCCURENCE OF INFECTION TIME SINCE TRANSPLANT IN LOWER RESPIRATORY TRACT INFECTED PATIENTS:

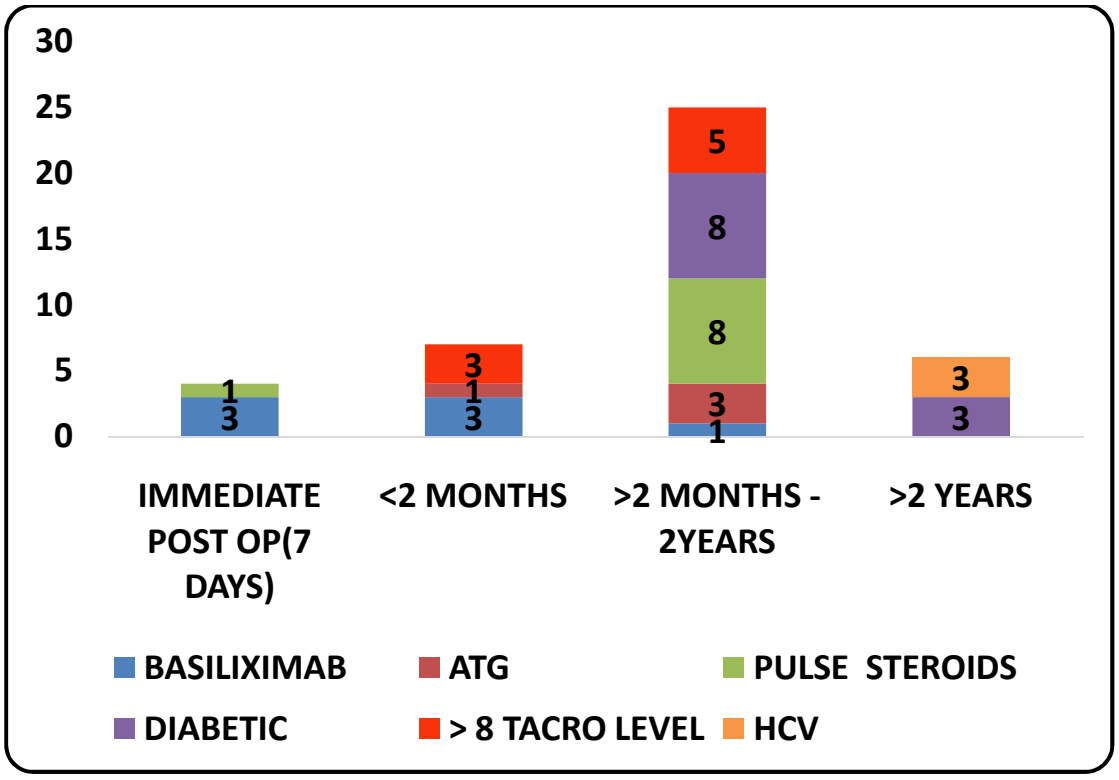
Table 31

Time interval of infection	Basilixi mab received	Atg received	Pulse steroids	Diabetic	> 8 tacro level	Hcv
Immediate post op(7 days)	3	0	1	0	0	0
<2 months	3	1	0	0	3	0
>2 months - 2years	1	3	8	8	5	0

>2 years	0	0	0	3	0	3

Patients who received basiliximab had infection in the period <2 months time since transplant whereas patients who received ATG, who had diabetes, pulse steroids for rejection, >8ng/ml of tacrolimus had infection more in the period of >2 months to 2 years. Patients who had HCV had pneumonia > 2 years of transplant.

Figure 13



DISCUSSION

Prevalence :

The prevalence of pneumonia in post renal transplant recipients in our study is about **27.2%** which correlates with the previous studies conducted by Gasink LB & colleagues, Kutinova A et al & Tveit et al 7,8,9 which says was about 2.9%- 30%. The rate is on the higher side as India is a developing country and a number of factors like unhygienic conditions, poor socio economic status and illiteracy play an

important role in increasing the infection rate. The patients have increased exposure to environmental respiratory pathogens and poor socio economic status leading to malnutrition thus increasing the net immunosuppression in addition to the immunosuppressive drugs. (according to Rubin et al [33]).

Gender difference:

Males constitute 85% (n=34)of the lower respiratory tract infection compared to females(n=6) which is about 15%. The difference is statistically significant **(p=<0.001).**This correlates with the study conducted in Nizam institute of medical science, Hyderabad [13]. 40.5% of the male transplant recipients had LRTI and 10% of the female transplant recipients had LRTI .The increase in incidence in males is due to their frequent outdoor activities (increased environmental exposure)[33] more than females .Hence are exposed frequently to environmental pathogens.

Age distribution:

` In our study ,pneumonia is more prevalent in the age group of 21-40 years (77.5%) which is similar to that in the study conducted in Nizam institute of medical science, Hyderabad [13] . The mean age is 32 in our study.

Lower respiratory tract infection rate based on donor type:

In our study, percentage of lower respiratory tract infection is more in live related transplant recipient patients (31.55%) compared to cadaver transplant recipients (25.8%).Among the total 40 lower respiratory tract infected patients , most

of the infection occurred in live related transplant patients (57.5%) compared to cadaveric transplant recipients (37.5%). But there is no statistical significance between the two groups (P=0.33) for the occurrence of lower respiratory tract infection.

Risk factors such as Basiliximab ,ATG , increased tacrolimus level are associated more with cadaver transplants. Whereas anti rejection therapies, diabetes were more with live related transplant patients. Since there is a statistical significance between anti rejection therapy (iv pulse steroids) and bacterial infection , the live related transplant recipients are at more risk of bacterial infection.

Types of infection among the lower respiratory tract infection patients:

Bacterial pneumonia:

In our study , bacterial infection is the most common infection (40%) than other infection among the lower respiratory tract infected transplant recipients.. This correlates with the independent studies conducted by Alangaden GJ, Bonatti H, Cervera C, Singh N et al [21,22,23,24].The bacterial pneumonia infection in our study in renal transplants is about 10.88%(n=16) which is higher than in the study by Nina Singh, M.D. and his colleagues which is about 4-5%. This is because of the poor hygiene, lower socio economic status of the people prevailing in developing countries which adds to the increased percentage in Indian population.

The incidence of bacterial pneumonia peaked in the initial 4-8 weeks which is about 43.75% (n=7) which correlates with what is said by Nina Singh N and his colleagues(35-48%). This is because of the intense immunosuppression the patient had received during this period that is the induction agents, increased dose of the maintenance triple drug regimen and anti rejection therapies if occurred.

In our study in the postoperative period Amp C producing Pseudomonas(n=1), carbapenamase producing acinetobacter (n=1), Methicillin resistance Staph aureus(n=1) are the organisms causing the infection. This clearly states these are nosocomially acquired. Gram negative organisms are more than gram positive organisms in the postoperative period. This correlates with the type of organism isolated mentioned in these studies.[25,10]

In our study, after the initial post operative period organisms which caused bacterial pneumonia were Haemophillus influenza , Klebsiella spp , Pseudomonas spp , Staphylococcus aureus . This correlates with the study by Nina Singh 25.These may me mostly community acquired. Resistance pattern is comparatively low when compared to organism isolated in the initial post transplant period.

There is no incidence of nocardia pneumonia in our study. This may be because of the lifelong prophylaxis of cotrimoxazole given to the transplant recipients for Pneumocystis carinii.

The **risk factors** associated with bacterial infection were basiliximab(n=3, P=0.48), Anti thymocyte globulin (n=1, P=0.74), pulse steroids for rejection therapy (n=6, P=0.03), diabetes (n=3, P=0.84), tacro level >8ng/ml (n=4, P=0.25). Induction

agents and increased tacrolimus level were associated in the earlier period whereas pulse steroids and diabetes were associated in the later period. **Intravenous pulse methyl prednisolone** administration for rejection given to the patients is **statistically associated** with **bacterial infection** in our study**(P=0.03).** All these patients except one (cadaver transplant- not received induction agent) are live related transplant recipients who had not received any induction agents. Hence antirejection therapy has statistical significance with bacterial infection since the immunosuppression is very much intensified during the period.

Resistance pattern of the bacterial organisms isolated:

In the immediate postoperative period , multidrug resistant organisms were found since the patient is exposed to hospital environment. Resistance is comparatively low in the intermediate and later period. Most of the organisms isolated showed resistance to cotrimoxazole since patient had been on lifelong prophylaxis for Pneumocystis carinii pneumonia.

Pulmonary tuberculosis:

In our study, **8.1%** (n=12)of the transplant patients are affected with pulmonary tuberculosis. This is higher than the percentage in the study conducted in Nizam institute of medical sciences (1.6%) [38] Pulmonary tuberculosis contributes 30% of the lower respiratory tract infection in our study .The median age to develop tuberculosis is **27 months**. This nearly correlates with the study conducted by JIA Liu et al which is about 20 months.[38] Majority of tuberculosis cases had occurred after one year (n=8) in our study (66.66%). This contradicts with these studies [42,43,44]

which says the majority of tuberculosis cases had occurred within one year of transplant. This may be because, the net state of immunosuppression is determined by the sustained level of immunosuppression the patient had rather than the dosage of the drug given during that period.[33]

Coming to the risk factors associated with the patients affected with pulmonary tuberculosis, Anti thymocyte globulin was received by 2 patients, intravenous pulse methyl prednisolone 3-5 doses for rejection were received by 4 patients, diabetes was associated with 4 patients, >8 ng/ml of tacro level was seen in 1 patient and HCV was seen in 1 patient. When Tuberculosis occurred within one years , the risk factors associated are Anti thymocyte globulin (P=0.17), intravenous pulse methyl prednisolone (P=0.40), diabetes (P=0.2), >8 ng/ml of tacrolimus level (P=0.88). Basiliximab received patients had no incidence of pulmonary Tb in our study. When tuberculosis occurred after one year, diabetes and HCV (P=0.44) are the risk factors associated in our study. Though these risk factors are said to be associated with the development of Tuberculosis in various studies [26, 45,46,49,48] there is no statistical significance between these risk factors and the development of pulmonary tuberculosis in our study. There is no statistical significance for the occurrence of pulmonary TB between diabetes under control and uncontrolled . Upper lobe of the lung is the mostly affected in tuberculosis in our study 53.33%.

Fungal pneumonia:

The incidence of fungal pneumonia in our study is **3.4%** (n=5) which correlates with the study by Alangaden GJ, Sileri P et al which says is about 1-4%. [21,27]. The mortality rate is about 40% (n=2) in our study. Aspergillus is the common organism in

our study (60%) (n=3) followed by mucor species (40%) (n=2). The mortality rate is 66.66% (n=2). Most of the fungal infection has occurred after 3 months of transplantation 80% (n=4). This is contradictory with the study by Gavalda et al [28] (majority of cases occurred within 90 days) but correlates with the occurrence of opportunistic infection in this period described by Rubin et .al[33].

The **risk factors** associated with fungal pneumonia in our study were basiliximab (n=2), 2-3 doses of intravenous pulse methyl prednisolone as antirejection therapy (n=2) , uncontrolled diabetes (n=4), HCV (n=1), tacrolimus level of 18.8 ng/ml (n=1). Basiliximab and high tacrolimus level are associated with fungal infection within 2 months of transplant whereas diabetes and HCV are associated with latter infection.

All the diabetic patients who had fungal infection had uncontrolled hyperglycemia(100%).Glycemic status of the diabetic patient had been an important factor in our study. There is a **statistical significance between diabetes and fungal pneumonia in our study (P=0.002).** Though intensified immunosuppression , anti rejection therapies, chronic viral infection such as HCV were stated as risk factors for fungal infection in transplant recipients in these studies [28,31] there is no statistical significance in our study. In our study one patient had both tuberculosis and fungal pneumonia and two patients had both bacterial and fungal pneumonia.

Most common lobe affected in fungal pneumonia patients is the upper lobe 80%. There is no incidence of Pneumocystis carinii reported in our patients. This is due to the lifelong prophylaxis of Cotrimoxazole given for the patients.

Cytomegalovirus pneumonia:

In our study , one case of Cytomegalovirus pneumonia was reported (0.68%). But the case was a late onset CMV (4.5 years since transplant). The viral load was about 1,23,254copies/ml in the plasma. Owl's eye intra nuclear inclusion bodies were positive from the lung biopsy sample. The risk factor associated were diabetes and Azathioprine based regimen for the patient. pp65 antigenemia for other patients suspected to have CMV were negative.

Other viral and atypical pneumonia:

Though a number of viruses other than CMV and atypical organisms cause pneumonia in transplant recipients, due to limitations in availability of investigations, it is not done in our study and hence comment about viral and atypical pneumonias could not be made out. In our study, in 11 patients, organisms could not be obtained though the patients had signs and symptoms suggestive of pneumonia. These could be due to these organisms.

Basiliximab:

A total of 20 patients had received Basiliximab among the total 147 patients. The rate of lower respiratory tract infection among Basiliximab received patients in our study is about 35%(n=7). In our study 85.7%(n=6) of the Basiliximab received patients had lower respiratory tract infection within 2 months. Basiliximab saturates IL- 2 receptors for 4-6 weeks14. No incidence of TB is reported in Basiliximab received patients.

According to the various studies conducted, there is no increase noted in the incidence of CMV, fungal and bacterial infections for Basiliximab when compared to placebo or other therapies for induction [18,19,20]. Our study also correlates with these studies since there is **no statistical significance** in the occurrence of lower respiratory tract infection (P=0.8) with the administration of Basiliximab. There is no statistical significance in the incidence of bacterial (P=0.48) and fungal infection(P=0.07) in Basiliximab received patients in our study.

Anti Thymocyte Globulin:

A total of 9 patients had received ATG as induction agent. The rate of lower respiratory tract infection is 44.44% (n=4) in these patients. 2 patients had pulmonary tuberculosis. Though lymphocyte depleting agents are considered as risk factors associated with tuberculosis in renal transplant recipients in these studies [45,46,49] there is no statistical significance in the occurrence of tuberculosis in ATG received patients in our study (P=0.17). In the study conducted by Midtvedt K et al ,ATG has been associated with increased incidence of pneumonia, bacteremia or sepsis . [56] But there is **no statistical significance** between ATG induction and bacterial infection in our study (P=0.74). Our study correlates with the study conducted by Chinese from Feb. 2007 to Jul. 2012 which says there is no increase in incidence of infection in patients received ATG since there is no statistical significance between ATG and lower respiratory tract infection in our study (P=0.88%). According to the study by Steven D. Burdette et al ,ATG induction in renal transplants does not lead to any increase in incidence of fungal infection.[14] This correlates with our study as there is no incidence of fungal pneumonia in our study.

Comparison between Basiliximab and ATG:

The rate of lower respiratory tract infection occurred is more in ATG (44.44%) than Basiliximab (35%) in our study. But there is **no statistical significance** between the two (P=0.68) in causing lower respiratory tract infection. This correlates with the study conducted by Chinese 16 from Feb 2007- 2012 (P>0.05) . But contradicts with the study conducted by Brennan DC et al [18.]

Intravenous pulse methyl prednisolone for anti rejection:

In our study , 22.5% of the lower respiratory tract infection patients had received pulse steroids as anti rejection therapy. In our study, it was associated with highest bacterial infection rate (66.66%). There is a **statistical significance between anti rejection therapy pulse steroids and bacterial pneumonia in our study (P=0.002).** The mean duration between administration and pneumonia is about 18 months in our study**.** In our study, the patients who received anti rejection therapy were live related transplants and did not receive any induction agents . There is an indirect association between rejection and bacterial pneumonia . There is no statistical significance between fungal and tuberculosis infection (P=0.4) related to pulse steroids (P=0.5%) in our study though it is considered as risk factor in these studies [45,46,47, 28]. In our study, 88.88% of the patients who received anti rejection therapy had pneumonia within 2 years of transplant .

Diabetes (including NODAT):

In our study, 11 patients with respiratory tract infection had diabetes (including 10 NODAT + 1 pre transplant DM). In our study, the lower respiratory tract infection

rate among diabetes patients is 27.5%. But there is **no statistical significance between pneumonia and diabetes in our study (P=0.73)**. The percentage of tuberculosis (36.36%) and fungal pneumonia (36.36%) is more than bacterial pneumonia (27.27%) in our study. Diabetes had **statistical significance with fungal pneumonia in our study (P=0.001).** This correlates with the study by [31,32]. All the patients with fungal pneumonia who are diabetic had poorly controlled diabetes and patients who have diabetes under control had no incidence of fungal infection .This correlates with the study by Bhansali et al [62] . Though diabetes is considered a risk factor **for tuberculosis(P=0.2) and bacterial infection (P=0.84)** in various studies by John GT et al in transplant recipients [48], there is no statistical difference in our study.

In our study 72.72% (n=8) of the patients who had diabetes , the infection occurred after 1 year of transplant. In our study 4 patients with diabetes had received pulse steroids for rejection , 2 had ATG, 1 had Basiliximab. In patients who received ATG and had NODAT, the infection occurred within 1 year of transplant. One patient with diabetes had CMV infection.

HCV infection:

In our study, 7.5% of the lower respiratory tract infection patients had HCV infection(n=3) .All had pneumonia after 5 years of transplant. This correlates with Rubin et all [33] study which says patients with chronic infection with immunomodulating virus such as HBV, HCV etc present with secondary infection in the later period. There is no statistical significance between HCV and bacterial (n=0)

, fungal (P=0.12) and tuberculosis (P=0.44) infection in our study though it is considered as risk factors in various studies [45,46,49,31].

Increased Tacrolimus level:

In our study 20% of the patients with lower respiratory tract infection had Tacrolimus level >8ng/ml at the time of infection. There is no statistical difference between increased trough level of Tacrolimus and bacterial (P=0.25), fungal (P=0.5), tuberculosis (P=0.88) infection at the time of infection. This is because the infection is directly related to duration of sustained immunosuppression rather than the duration of the dose at a particular time by Rubin et al [33]. We rather need to study about the duration the patient had exposed to higher Tacrolimus level which will give a better idea if the Tacrolimus level is influencing the occurrence of pneumonia. Since all the patients are receiving Tacrolimus in the triple drug maintenance regimen, individual attribute of the drug to a particular infection cannot be made out . Only the trough level of the drug can be correlated to infection.

MMF and oral prednisolone:

Since all renal transplant recipients received MMF and oral prednisolone as a part of triple drug maintenance therapy lifelong and their serum levels are not monitored, risk of infection associated independently with these drugs could not be made out in our study.

TIME SINCE TRANSPLANT:

Early post transplantation period: <2 months/period of intense immune suppression:

Bacterial pneumonia is the most common infection during this period in our study. And the bacterial organisms isolated in the immediate post operative period are nosocomial acquired and are multidrug resistant. Only one case of opportunistic fungal infection was seen in our study within 2 months. The patient must had intense immunosuppression since the tacrolimus level was 18.8ng/ml and had basiliximab for induction. Basiliximab is the risk factor most commonly associated within this period. Here the patient's pretransplant status and the duration of surgery, surgical skills, nosocomial exposure to pathogens play a role in addition to the immunosuppression given by the drugs.

Intermediate period :>2months - 2year period:

Most of the lower respiratory tract infection had occurred during this period(40%). This is because of the sustained immunosuppression the patient had exposed to. During this period, community acquired pathogens such as tuberculosis, Haemophillus and opportunistic fungal infection has caused increased incidence of pneumonia in our study. Diabetes and pulse steroids for rejection the patient had received were the major risk factors found in patients who had pneumonia during this period.

Late post transplant period (>2 years):

During this period tuberculosis, opportunistic fungal infection causing pneumonia is mostly found. The risk factors found are immunomodulating virus HCV and diabetes.

Limitations of Rubin's table for present application:

The study was conducted in the year 1998. The study was based mostly on the tacrolimus or cyclosporine based regimen. The table concludes a risk of infection more in the period of 1-6 months. But in our study it was more in the period of 1 to 2 years. Since no induction therapies were used during this period , the table cannot be applied as such and slighter modifications were needed for the time interval. This is also concurred by the study conducted in Nizam Institute of Medical Sciences of Hyderabad which showed increased risk of infection from 1 to 3 years. [13]

SUMMARY

This study was conducted to find the prevalence of lower respiratory tract infections in post renal transplants in a tertiary care hospital between September 2014 to August 2015. From a total of 147 patients, 40 patients had lower respiratory tract infections . The details of some patients were collected retrospectively and for the other patients processing is done to find out the type of organism.

The prevalence of lower respiratory tract infection in renal transplant recipients in our study is about 27.2%. It is more common in males (39.08%) compared to females (10%) due to increased environmental exposure (P=<0.001). It is more common in 20-40 yrs of age group (77.5%).Though the percentage of pneumonia is more common in live related transplant recipient patients compared to cadaveric transplant recipients , there is no statistical significance between the two (P=0.33).

Bacteria (40%) is the most common cause of pneumonia in our study followed by tuberculosis (30%) , fungal pneumonia (12.5%) and CMV (2.5%).

The rate of bacterial pneumonia is 10.8%, the rate of pulmonary tuberculosis is 8.16%, the rate of fungal pneumonia is 3.4% and CMV is 0.68% among the total renal transplant recipients

Cadaveric transplant recipients are associated with more risk factors than live related transplants. But pulse steroids are more in live related transplants. Diabetes (27.5%) is the leading risk factor associated with lower respiratory tract infection patients (27.5%) , followed by pulse steroids (22.5%) which is given for rejection.

In the association of specific risk factors with specific infection by proportion test, only pulse steroids given for rejection had statistical significance with bacterial pneumonia (P=0.03) and diabetes had statistical significance with fungal pneumonia (P=0.002). The rate of lower respiratory tract infection occurred is more in ATG (44.44%) than Basiliximab (35%) but there is no statistical significance between the two (P=0.68)

Basiliximab (P=0.8) , ATG (P=0.88), Diabetes (P=0.73) had no statistical significance with lower respiratory tract infection in renal transplant recipient patients.

Aspergillus and Mucor were the fungal species causing pneumonia in our study. Fungal pneumonia had a mortality rate of 66.66% in our study. All the diabetes patients with fungal pneumonia (n=4) had poorly controlled glycemic status.

Most of the lower respiratory tract infection had occurred in the duration of >2 months to 2 years (40%) after transplantation. Up to 1 year time since transplant, lower respiratory infection was more common in cadaveric transplant recipients (60%). After 1 year , it was common in live related transplant recipients (80%).

In our study, bacterial pneumonia peaked in the period of <2 months time since transplant whereas tuberculosis and fungus pneumonia were commonly found in the period of >2 months to 2 years.

Patients who received Basiliximab had infection in the period <2 months time since transplant whereas patients who received ATG, who had diabetes, pulse steroids for rejection, >8ng/ml of Tacrolimus had infection more in the period of >2 months to 2 years. Patients who had HCV had pneumonia > 2 years of transplant.

Nosocomially acquired multidrug resistant bacterial organisms dominated during the earlier post transplant period followed by community acquired tuberculosis, other bacterial organisms and opportunistic fungal organisms in the intermediate and later period.

CONCLUSION

The prevalence of lower respiratory tract infection in renal transplant recipients in our hospital is about 27.2%.

There was a higher incidence of fungal pneumonia in poorly controlled diabetes patients.

Patients who received intravenous pulse methyl prednisolone for rejection had higher incidence of bacterial infection.

Induction therapy was not associated with increase in incidence of infection.

Since patient is on lifelong prophylaxis of cotrimoxazole, there is a higher increase of resistance to it.

FUTURE PROSPECTIVE:

Since anti rejection therapy in renal transplant recipients had statistical significance with the association of bacterial infection and those patients had not received induction agents, a comparative study for the occurrence of infection between patients who received induction agents and not received need be done.

Since the median time to develop pneumonia is 18 months from the administration of intravenous pulse steroids for rejection, other infections associated with their administration have to be studied in detail.

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34. ∗Corresponding Author: Michael Green, Michael.green@chp.edu Introduction: Infections in Solid Organ Transplantation M. Green∗ Department of Pediatrics, Surgery & Clinical and Translational Science, University of Pittsburgh School of Medicine. Division of Infectious Diseases, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA American Journal of Transplantation 2013; 13: 3–8

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KEY TO MASTER CHART:

SNO=SERIAL NO

AGE= AGE INTERVAL

A=10-20 YEARS

B=21-30YEARS

C=31-40YEARS

D=41-50YEARS

DONOR=DONOR TYPE

C=CADAVER

L=LIVE RELATED

S=SPOUSAL

PERIOD=TIME OF INFECTION OCCURED

IND=INDUCTION AGENT RECEIVED

BAS=BASILIXIMAB

ATG=ANTI THYMOCYTE GLOBULIN

PUL=PULSE STEROIDS

DM=DIABETIC

UNCON=UNCONTROLLED DIABETES

>8 TACRO= >8ng/ml LEVEL OF TACROLIMUS

NA=NOT APPLICABLE

SNO	AGE	DONOR	PERIOD	IND	PULSE	DM	UNCON	>8 TACRO	TB	FUNGUS	BACTERIA
1	D	C	M	BAS	NN	NO	NA	NA	NO	NO	NO
2	B	C	M	BAS	NN	NO	NA	NA	NO	NO	NO
3	C	C	M	BAS	NN	NO	NA	NA	NO	NO	YES
4	C	C	M	NO	NN	NO	NA	NA	NO	NO	NO
5	B	L	M	NO	PUL	NO	NA	NA	NO	NO	YES
6	D	L	M	NO	NN	NO	NA	NA	NO	NO	YES
7	B	L	M	NO	NN	NO	NA	NA	NO	NO	NO
8	B	C	N	ATG	NN	NO	NA	NA	NO	NO	YES
9	B	L	N	NO	NN	NO	NA	NA	NO	NO	YES
10	C	S	N	BAS	NN	NO	NA	YES	NO	YES	NO
11	D	C	N	BAS	NN	NO	NA	YES	NO	NO	YES
12	B	C	N	BAS	NN	NO	NA	NA	NO	NO	NO
13	C	C	O	NO	PUL	YES	YES	NA	YES	YES	YES
14	B	C	O	NO	NN	NO	NA	YES	YES	NO	YES
15	B	L	O	NO	PUL	NO	NA	NA	YES	NO	YES
16	C	C	O	ATG	NN	YES	YES	YES	NO	NO	NO
17	D	C	O	ATG	NN	YES	NA	NA	YES	NO	NO

18	A	L	O	NO	PUL	NO	NA	NA	NO	NO	NO
19	B	C	O	NO	NN	NO	NA	YES	NO	NO	YES
20	A	L	O	NO	NN	NO	NA	NA	NO	NO	NO
21	B	L	O	NO	PUL	YES	YES	NA	NO	YES	YES
22	C	L	O	NO	PUL	NO	NA	YES	NO	NO	YES
23	B	L	O	NO	NN	NO	NA	NA	NO	NO	YES
24	D	L	O	NO	NN	YES	NA	YES	NO	NO	NO
25	C	C	O	NO	PUL	YES	NA	NA	NO	NO	YES
26	B	L	O	NO	NN	YES	NA	NA	YES	NO	NO
27	D	S	O	BAS	NN	YES	YES	NA	NO	YES	NO
28	B	L	O	ATG	PUL	NO	NA	NA	YES	NO	NO
29	B	C	P	NO	NN	NO	NA	NA	NO	NO	NO
30	C	L	P	NO	NN	NO	NA	NA	YES	NO	NO
31	B	L	P	NO	NN	NO	NA	NA	NO	NO	NO
32	C	L	P	NO	NN	NO	NA	NA	YES	NO	NO
33	C	C	P	NO	NN	NO	NA	NA	YES	NO	NO
34	C	L	P	NO	NN	NO	NA	NA	YES	NO	NO
35	C	L	P	NO	NN	YES	YES	NA	NO	NO	NO
36	B	L	P	NO	NN	NO	NA	NA	YES	NO	YES
37	C	L	P	NO	NN	NO	NA	NA	NO	NO	YES
38	C	L	P	NO	NN	YES	NA	NA	NO	YES	NO
39	B	L	P	NO	NN	NO	YES	NA	NO	NO	NO
40	C	L	P	NO	NN	YES	NA	NA	YES	NO	NO
41	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
42	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
43	C	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
44	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
45	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
46	A	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
47	B	C	NA	ATG	NN	YES	NA	NA	NO	NO	NO
48	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
49	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
50	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
51	B	C	NA	BAS	NN	NO	NA	NA	NO	NO	NO
52	C	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
53	D	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
54	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
55	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
56	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
57	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
58	B	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
59	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
60	A	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
61	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
62	C	C	NA	BAS	NN	NO	NA	NA	NO	NO	NO

63	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
64	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
65	D	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
66	B	C	NA	ATG	NN	NO	NA	NA	NO	NO	NO
67	C	S	NA	NO	NN	YES	NA	NA	NO	NO	NO
68	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
69	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
70	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
71	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
72	A	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
73	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
74	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
75	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
76	D	C	NA	NO	NN	YES	NA	NA	NO	NO	NO
77	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
78	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
79	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
80	D	S	NA	NO	NN	NO	NA	NA	NO	NO	NO
81	B	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
82	A	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
83	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
84	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
85	B	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
86	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
87	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
88	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
89	C	C	NA	ATG	NN	YES	NA	NA	NO	NO	NO
90	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
91	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
92	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
93	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
94	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
95	D	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
96	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
97	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
98	B	S	NA	NO	NN	NO	NA	NA	NO	NO	NO
99	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
100	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
101	C	C	NA	NO	NN	YES	NA	NA	NO	NO	NO
102	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
103	A	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
104	C	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
105	B	C	NA	NO	NN	YES	NA	NA	NO	NO	NO
106	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
107	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO

108	D	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
109	B	C	NA	BAS	NN	YES	NA	NA	NO	NO	NO
110	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
111	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
112	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
113	C	C	NA	ATG	NN	NO	NA	NA	NO	NO	NO
114	B	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
115	D	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
116	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
117	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
118	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
119	C	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
120	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
121	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
122	D	S	NA	NO	NN	NO	NA	NA	NO	NO	NO
123	C	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
124	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
125	D	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
126	A	C	NA	ATG	NN	YES	NA	NA	NO	NO	NO
127	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
128	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
129	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
130	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
131	A	C	NA	BAS	NN	YES	NA	NA	NO	NO	NO
132	C	S	NA	NO	NN	NO	NA	NA	NO	NO	NO
133	D	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
134	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
135	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
136	B	S	NA	BAS	NN	YES	NA	NA	NO	NO	NO
137	C	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
138	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
139	A	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
140	D	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
141	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
142	C	L	NA	NO	NN	YES	NA	NA	NO	NO	NO
143	B	S	NA	BAS	NN	NO	NA	NA	NO	NO	NO
144	B	C	NA	NO	NN	NO	NA	NA	NO	NO	NO
145	C	L	NA	NO	NN	NO	NA	NA	NO	NO	NO
146	D	C	NA	NO	NN	YES	NA	NA	NO	NO	NO
147	B	L	NA	NO	NN	NO	NA	NA	NO	NO	NO

Name: Age: Sex:

Occupation: Nephro no:

Donor: Cadaver Live related- Live unrelated

Blood group of Recipient : Blood group of Donor:

HLA typing: Cross match % :

Associated medical conditions if any:

Date of Transplant: Duration from the date of transplant done:

Rejection episodes :

Any induction agent given in POP:

Current Immunosuppressive regimen followed and other drugs:

Any alteration in the dose of immunosuppressive regimen before:

Last 3 Tacrolimus levels:

1.

2.

3.

Present Total count:

Differential count: N- E- B- M- L-

Serum urea:

Serum creatine :

Complaints suggestive of lower respiratory tract infections:

Any X ray , CT findings suggestive of lower respiratory tract infections:

Type of specimen obtained:

Details of specimen obtained:

Colour:

Amount:

foul smelling : yes or no

RESULTS:

Direct grams stain:

Acid fast staining:

KOH mount:

Bacterial culture:

Organism obtained :

Sensitivity pattern:

Fungal Culture:

Organism obtained:

Sensitivity:

Viral report:

Blood culture report if taken:

AWÑ vPôu- UÚjÕYd Lpí¬, ùNuû] - 600 001.

TeÏ ùTßTY¬u J¦Tm

BWônf£ SûPùTßm CPm : AWÑ vPôu- UÚjÕYdLpí¬ ùNuû]

TeÏ ùTßTY¬u

ùTVÚm ØLY¬Ùm :

Sôu ..... CkR BWônf£«u ®YWeLû[G]Õ ùNôkR ùUô¯«p á\ A±kÕ ùLôiúPu.

CkR BWônf£«u ØÝ®YWeLû[Ùm Sôu A±kÕ ùLôiúPu. CkR BWônf£«p Sôu TeÏùTßm úTôÕ G]dÏ HtTÓm SuûU ¾ûULû[ØÝYÕUôL A±kÕ ùLôiúPu.

CkR BWônf£«u úTôÕ GlúTôÕ úYiÓUô]ôÛm Sôu ®X¡d ùLôs[Xôm GuTûRÙm, AR]ôp G]dÏ ¡ûPdÏm UÚjÕYj§p GkR®R Uôt\úUô Tô§lúTô CÚdLôÕ Gußm A±úYu. CkR BWônf£«p Sôu TeÏùTßYRtLôL Sôu GkR®R NuUô]Øm (TQUôLúYô, ùTôÚ[ôLúYô) YôeLUôhúPu. CkR BWônf£«u Ø¥ÜLû[, Gu AûPVô[eLû[Ï±l©PôUp UÚjÕY CRrL°p ùY°«P G]dÏ GkR BhúNTû]Ùm CpûX. CkR BWônf£«p Gu TeÏ Gu] GuTûR A±úYu. CkR BWônf£dÏ G]Õ ØÝ JjÕûZlûTÙm RÚúYu Guß Eß§ A°d¡ú\u.

TeÏ ùTßTY¬u ùTVÚm ØLY¬Ùm :

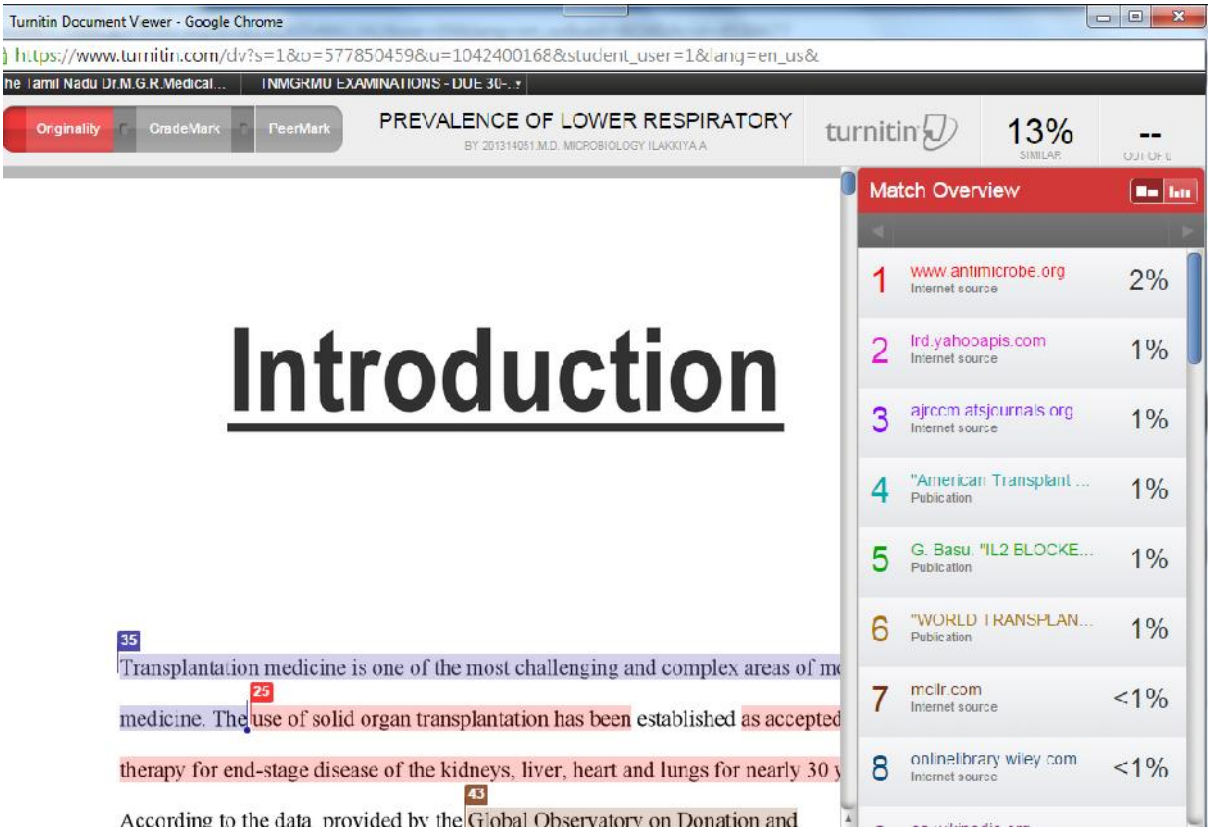
TeÏ ùTßTY¬u ûLùVôlTm / ®WpúWûL :

úR§ :

Nôh£ :

(Nôh£«u ùTVo, ØLY¬, ûLùVôlTjÕPu)

BWônf£ ùNnTY¬u ùTVÚm ûLùVôlTØm: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Introduction
Transplantation medicine is one of the most challenging and complex areas of
medicine. The use of solid organ transplantation has been established as accepted
therapy for end-stage disease of the kidneys, liver, heart and lungs for nearly 30
According to the data provided by the Global Observatory on Donation and